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AIR QUALITY CRITERIA FOR CARBON MONOXIDE

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U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Environmental Health Service

179

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U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Environmental Health Service
National Air Pollution Control Administration
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PREFACE

Air quality criteria tell us what science has thus far been able to measure of the obvious as well as the insidious effects of air pollution on man and his environment. Such criteria provide the most realistic basis that we presently have for determining to what point pollution levels must be reduced if we are to protect the public health and welfare.

The criteria we can issue at the present time do not tell us all that we would like to know; but taking all of man's previous experience in evaluating environmental hazards as a guide, we can conclude that improved knowledge will show that there are identifiable health and welfare hazards associated with air pollution levels that were previously thought to be innocuous. As our scientific knowledge grows, air quality criteria will have to be reviewed and, in all probability, revised. The Congress has made it clear, however, that we are expected, without delay, to make the most effective use of the knowledge we now have.

The 1967 amendments to the Clean Air Act require that the Secretary of Health, Education, and Welfare". . .from time to time, but as soon as practicable, develop and issue to the States such criteria of air quality as in his judgment may be requisite for the protection of the public health and welfare . . . Such criteria shall . . . reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of an air pollution agent . . . ."

Under the Act, the issuance of air quality criteria is a vital step in a program designed to assist the States in taking responsible technological, social, and political action to protect the public from the adverse effects of air pollution.

Briefly, the Act calls for the Secretary of Health, Education, and Welfare to define the broad atmospheric areas of the Nation in which climate, meteorology, and topography, all of which influence the capacity of air to dilute and disperse pollution, are generally homogeneous.

Further, the Act requires the Secretary to define those geographical regions in the country where air pollution is a problem—whether interstate or intrastate. These air quality control regions will be designated on the basis of meteorological, social, and political factors which suggest that a group of communities should be treated as a unit for setting limitations on concentrations of atmospheric pollutants. Concurrently, the Secretary is required to issue air quality criteria for those pollutants he believes may be harmful to health or welfare, and to publish related information on the techniques which can be employed to control the sources of those pollutants.

Once these steps have been taken for any region, and for any pollutant or combination of pollutants, then the State or States responsible for the designated region are on notice to develop ambient air quality standards applicable to the region for the pollutants involved, and to develop plans of action for implementing the standards.

The Department of Health, Education, and Welfare will review, evaluate, and approve these standards and plans and, once they are approved, the States will be expected to take action to control pollution sources in the manner outlined in their plans.

At the direction of the Secretary, the National Air Pollution Control Administration has established appropriate programs to carry out the several Federal responsibilities specified in the legislation. Previously, on February 11, 1969, air quality criteria and control techniques information were published for sulfur oxides and particulate matter.

This publication, *Air Quality Criteria for Carbon Monoxide,* is the result of extensive and dedicated effort on the part of many persons–so many that it is not practical to name each of them.

In accordance with the Clean Air Act, a National Air Quality Criteria Advisory Committee was established, having a membership broadly representative of industry, universities, conservation interests, and all levels of government. The committee provided invaluable advice on policies and procedures under which to issue criteria, and provided major assistance in drafting this document.

With the help of the committee, expert consultants were retained to draft portions of this document, while other segments were drafted by staff members of the National Air Pollution Control Administration. After the initial drafting, there followed a sequence of review and revision by the committee, as well as by individual reviewers especially selected for their competence and expertise in the many fields of science and technology related to the problems of atmospheric pollution by carbon monoxide. These efforts, without which this document could not have been completed successfully, are knowledge individually on the following pages.

As also required by the 1967 amendments to the Clean Air Act, appropriate Federal departments and agencies, also listed on the following pages, were consulted prior to issuing this criteria document. A Federal consultation committee, comprising members designated by the heads of 17 departments and agencies, reviewed the document, and met with staff personnel of the National Air Pollution Control Administration to discuss their comments.

This Administration is pleased to acknowledge the efforts of each of the persons specifically named, as well as the many not named who have contributed to the publication of this volume. In the last analysis, however, the National Air Pollution Control Administration is responsible for its content.

JOHN T. MIDDLETON

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CHAPTER 1.

INTRODUCTION

Pursuant to authority delegated to the Commissioner of the National Air Pollution Control Administration, *Air Quality Criteria for Carbon Monoxide* is issued in accordance with Section 107(b) of the Clean Air Act (42 U.S.C. 1857-18571).

Air quality *criteria* are an expression of the scientific knowledge of the relationship between various concentrations of pollutants in the air and their adverse effects on man and his environment. Criteria are issued to assist the states in developing air quality standards. Air quality criteria are descriptive; that is, they describe the effects that have been observed to occur when the concentration of a pollutant in the ambient air has reached or exceeded a specific level for a specific time period. In the development of criteria, many factors have to be considered. The chemical and physical characteristics must be considered, along with exposure time and conditions of the environment. The criteria must also include consideration of the contributions of all such variables to the effects of air pollution on human health, agriculture, materials, visibility, and climate. Futher, the individual characteristics of the receptor must be taken into account. Table 1 - 1 is a list of the major factors considered in developing criteria.

Air quality *standards* are prescriptive. They prescribe pollutant exposure or levels of effect that a political jurisdiction determines should not be exceeded in a specified geographic area, and are used as one of several factors in designing legally enforceable pollutant emission standards.

This document focuses on carbon monoxide (CO) as it is found in the ambient air; therefore, literature on extremely high levels of CO has not been extensively cited. The occurrence, properties, and fate of atmospheric CO and principles of formation and control are reviewed in the earlier chapters; these are followed by a discussion of estimation of CO emissions and measurement of atmospheric CO. The effects of CO are considered in relation to (1) vegetation, (2) toxicological studies on animals and man, and (3) epidemiological studies.

The National Air Pollution Control Administration is currently advocating the use of the metric system to express atmospheric concentrations of air pollutants, e.g., micrograms per cubic meter ($\mu g/m^3$). In most instances, gaseous pollutants have hitherto been reported on a volume ratio basis, i.e., parts per million (ppm). In this document, wherever possible, both types of units are given. Conversion from volume (ppm) to mass ($\mu g/m^3$) units requires a knowledge of the gas density at the temperature and pressure of measurement, since gas density varies with changes in these two parameters. In this document 25°C (77°F) has been taken as standard temperature and 760 mm Hg (atmospheric pressure at sea level) as standard pressure.

Because of the magnitude of the numbers involved, concentrations of CO are given in milligrams per cubic meter rather than in micrograms per cubic meter. The factor for converting CO from volume (ppm) to mass (mg/m^3) units is given in Chapter 2. The Appendix includes information of the derivation of this factor.

In general, the terminology employed follows usage recommended in the publications style guide of the American Chemical Society.

The scientific literature has been generally reviewed through March 1969, with additional sources from reports as recent as January 1970. The results and conclusions of foreign investigations are evaluated for their possible application to the air pollution problem in the United States. This document is not intended as a complete, detailed literature review, and it does not cite every published article relating to CO in the ambient atmosphere. The literature has, however, been reviewed thoroughly for information related to the development of criteria; and the document not only summarizes the current scientific knowledge of CO air pollution, but also attempts to point up the major deficiencies in that knowledge and the presently recognized needs for further research.

Methods and techniques for controlling the sources of CO emissions as well as the costs of applying these techniques are described in AP-65, *Control Techniques for Carbon Monoxide from Stationary Sources* and AP-66, *Control Techniques for Carbon Monoxide, Nitrogen Oxide, and Hydrocarbon Emissions from Mobile Sources.*

Table 1–1. FACTORS TO BE CONSIDERED IN DEVELOPING AIR QUALITY CRITERIA[a]

- Properties of pollution
  - Concentration
  - Chemical composition
  - Mineralogical structure
  - Adsorbed gases
  - Coexisting pollutants
  - Physical state of pollutant
    - Solid
    - Liquid
    - Gas
  - Kinetics of formation
  - Residence time
- Measurement methods
  - Spectroscopic
  - Chemical
- Exposure parameters
  - Duration
  - Concomitant conditions
    - Temperature
    - Pressure
    - Humidity
- Characteristics of receptor
  - Physical characteristics
  - Individual susceptibility
  - State of health
  - Rate and site of transfer to receptor
- Responses
  - Effects on health (diagnosable effects, latent effects, and effects predisposing the organism to diseases)
    - Human health
    - Animal health
    - Plant health
  - Effects on human comfort
  - Soiling
  - Other objectionable surface deposition
  - Corrosion of materials
  - Deterioration of materials
  - Effects on atmospheric properties
  - Effects on radiation and temperature

[a] Adapted from S. Calvert. Statement for air quality criteria hearings held by the Subcommittee on Air and Water Pollution of the U.S. Senate Committee on Public Works. July 30, 1968. Published in "Hearings Before the Subcommittee on Air and Water Pollution of the Committee on Public Works, United State Senate (Air Pollution-1968, Part 2)."

CHAPTER 2.

OCCURRENCE, PROPERTIES, AND FATE OF ATMOSPHERIC CARBON MONOXIDE

A. INTRODUCTION

Carbon monoxide (CO) is the most widely distributed and the most commonly occurring air pollutant. Total emissions of CO to the atmosphere exceed those of all other pollutants combined.

Most atmospheric CO is produced by the incomplete combustion of carbonaceous materials used as fuels for vehicles, space heating, and industrial processing or burned as refuse. Man's activities are, therefore, largely responsible for CO contamination, and his technological advances have contributed to the present atmospheric concentrations.

No large natural source of CO has been positively identified, but a number of geophysical and biological sources of CO are known. Their ultimate contribution to urban atmospheric concentrations is thought to be relatively small.[1]

This document explores the fundamental knowledge on CO in the context of its role as an air pollutant; there are many other aspects of CO of collateral interest. In addition to the references to be found in this document, a bibliography[2] on CO compiled in 1966 gives sources of further information.

B. CARBON MONOXIDE IN HISTORY

Human experience with CO probably began during prehistoric times when man first discovered fire. CO poisoning has been traced through Greek and Roman literature; in fact, this form of poisoning has been closely associated with the history of mankind.

Materials used for making fire in prehistoric times were probably wood, grasses, and other organic matter. Lewin[3] cites many cases of CO poisoning due to the incomplete combustion of such fuels. He also includes references to the effects of CO on the health of man in the writings of Greek physicians of the Third Century.

With the increased use of coal for domestic heating in the Fifteenth Century, CO poisoning increased greatly. This increase was due to inhalation of CO formed in incomplete combustion in the heating of homes and to the exposure of men in mines where the deadly "white damp" was encountered after explosions and mine fires. The introduction of illuminating gas (a mixture of hydrogen, carbon monoxide, methane, and other hydrocarbons) for domestic heating (still used extensively in Europe but largely replaced by natural gas in the United States) further increased this hazard.

The introduction of the internal combustion engine for transportation and the development of a number of technological processes wherein CO is produced have greatly increased the production of CO and its release to the atmosphere.

Over the past few centuries, therefore, the problem of dealing with CO has spread from individual dwellings and work environments to include the ambient air in cities. Concern has now broadened from the acute and often lethal effects of high concentrations of the gas to encompass as well those effects that may occur as a result of considerably longer exposures to much lower concentrations.

C. OCCURRENCE

1. Technological Sources

Carbon monoxide is found among the combustion products of organic materials used as fuels. Transportation activities represent the largest source category. Other major technological sources of CO emissions are stationary heat-generating facilities, industrial processes, and solid-waste combustion. CO is also formed in explosions and in the firing of weapons. It occurs in high concentrations in cigarette smoke. The major technological sources of CO are discussed in greater detail in Chapter 4.

2. Natural Sources

a. *Nonbiological*

Some CO is reported to be produced in volcanos and is formed in natural gases (e.g., gases found in coal mines).[4] It has also been reported to be formed during electrical storms.[5] Forest fires caused by lightning sometimes make a considerable contribution to atmospheric CO.[6] A small amount of CO is also formed as a photochemical degradation product of various reactive organic compounds in the process involving the formation of photochemical smog.[7,8] Some CO is believed to be formed in the upper atmosphere above 70 kilometers (km) by photodissociation of carbon dioxide (CO_2).[9]

b. *Biological*

Small quantities of CO are formed by vegetation during seed germination and seedling growth of plants,[10] and it has been observed in injured, cut, or dried plants.[11] Some CO is found in marsh gases and it is also formed by certain brown algae (kelps).[12,13] Carbon monoxide concentrations of up to 900 milligrams per cubic meter (mg/m^3) (786 ppm) have been found in the floats of *Nereocyctis*, a familiar kelp or seaweed.[14] Mature leaves of green plants have been shown to produce CO.[11] Microorganisms also have shown to produce CO from plant flavonoids.[15]

Carbon-monoxide-producing colonies of marine hydrozoan jellyfish (siphonophores) are widespread and make up a large portion of the plankton in the warmer oceans of the world.[16,17] CO is also produced in the float cells of the surface-dwelling *Physalia physalis* (Portugese Man-of-War).[18] In addition to the generation of CO by ocean-dwelling biological specimens, other mechanisms may exist through which CO is generated in the ocean.

Another biological source of CO is endogenous CO, which is produced in measurable quantities in man and animals as a by-product of heme catabolism.[19-21] This endogenous Co is produced in larger amounts in hemolytic disease states.

D. PROPERTIES AND GASEOUS REACTIONS OF CARBON MONOXIDE

1. Physical Properties

Carbon monoxide is a colorless, odorless, tasteless gas, slightly lighter than air.[22] Quite flammable, it burns with a bright blue flame, but does not support combustion.

Physical properties of CO are outlined in Table 2–1.

2. Gaseous Chemical Reactions of Carbon Monoxide

The likely gaseous reactions wherein CO might be oxidized to CO_2 have been reviewed by Bates and Witherspoon.[9] The reaction with molecular oxygen:

$$2\,CO + O_2 \rightarrow 2\,CO_2 \qquad (1)$$

is possible in the lower atmosphere, but is apparently unimportant. Both dry and moist experimental mixtures of CO and oxygen have remained unchanged after 7 years of exposure to sunlight.[23] The possibilities of reactions between CO and atomic oxygen have been reviewed by Leighton,[8] and he has concluded that they are unimportant; Bates and Witherspoon have come to a similar conclusion.[9]

a. *Lower Atmospheric Reactions*

Two oxidation reactions, although very slow, do occur in the lower atmosphere.[24-26]

$$CO + O_2 \rightarrow CO_2 + O \qquad (2)$$

and in the presence of moisture

$$CO + H_2O \rightarrow CO_2 + H_2. \qquad (3)$$

Both of these reactions have appreciable energy barriers, 51 and 56 kilocalories per mole

Table 2-1. PHYSICAL PROPERTIES OF CARBON MONOXIDE

Molecular weight	28.01
Melting point	-207°C
Boiling point	-192°C
Specific gravity relative to air	0.968
Density	
At 0°C, 760 mm Hg	1.25 g/liter
At 25°C, 760 mm Hg	1.15 g/liter
Explosive limits in air	12.5 to 74.2% (volume)
Solubility[a]	
At 0°C	3.54 ml/100 ml water
At 25°C	2.14 ml/100 ml water
Conversion factors	
At 0°C, 760 mm Hg	1 mg/m^3 = 0.800 ppm 1 ppm = 1.250 mg/m^3
At 25°C, 760 mm Hg	1 mg/m^3 = 0.874 ppm 1 ppm = 1.145 mg/m^3

[a] Volume of CO indicated is at 0°C, 760 mm Hg.

(kcal/mole), respectively. Direct chemical reactions between CO and oxygen or water occur at a frequency of less than one reaction per 10^{15} molecular collisions at room temperature. These reactions become important as gas-phase processes primarily at temperatures above 500°C and even more so above 1000°C. These reactions occur more readily and at lower temperatures on the surfaces of certain catalysts, usually metal oxides. For example, oxidation is catalyzed at room temperatures by metallic catalysts, such as Hopcalite, which is a mixture of the oxides of manganese and copper, and by palladium on silica gel.[27]

Ozone will oxidize CO to CO_2, but the rate of this reaction is extremely slow at atmospheric temperatures and concentrations.[28,29] A high activation energy of about 20 kcal for the oxidation of CO by ozone has been found.[30]

Oxidation by NO_2 in the reaction

$$NO_2 + CO \rightarrow CO_2 + NO \qquad (4)$$

has an even higher activation energy than does the oxidation of CO by ozone. The activation energy of 28 kcal essentially precludes the occurrence of this process in the atmosphere.[31]

Consideration has also been given to the possibility that some very rapid reactions may occur between CO and certain intermediates of photochemical smog reactions. One possible intermediate is the hydroxyl radical, which may occur when the photolysis of aldehydes produces perhydroxyl, which can then be reduced to the hydroxyl radical. Hydroxyl appears to react very rapidly with CO, and there is some indication that perhydroxyl also reacts with CO.[32] Such reactions involve chain-type mechanisms, and Doyle[33] has calculated that a global average hydroxyl concentration of only 10^{-9} to 10^{-8} part per million (ppm) would be sufficient to convert all emitted CO to CO_2.

Methane, which is found in the troposphere at concentrations one order of magnitude higher than CO concentrations, can also be oxidized by hydroxyl radicals. The rate of reaction is slow, however, and the extent to which methane competes with CO for the hydroxyl radicals in the atmosphere has not been defined.

Although future research with hydroxyl radicals may be rewarding, at present one must conclude that significant gaseous oxidation reactions of CO in the ambient atmosphere have not been proved.

b. Upper Atmospheric Reactions

Short-wavelength ultraviolet radiation (about 1700Å) dissociates CO_2 into CO and atomic oxygen[9] according to the reaction:

$$CO_2 + h\nu \rightarrow CO + O. \qquad (5)$$

The yield of CO from the photodissociation of CO_2 in the upper atmosphere, however, is considered to be relatively small at levels below 100 kilometers since the intensity of active ultraviolet radiation falls off rapidly at that level.

Carbon dioxide may be reformed by a three-body collision:

$$CO + O + M \rightarrow CO_2 + M \qquad (6)$$

where M represents the third body. The third body absorbs excess energy by collision from the energy-rich combination of a CO molecule and an oxygen atom. In the absence of such a collision, no stable CO_2 can be formed. The probability of this collision occurring is small, however, because of the low concentration of such third bodies at higher altitudes.

From the foregoing information, it must be concluded that no gaseous reactions have been shown to be important scavengers of CO in the atmosphere.

E. BACKGROUND LEVELS AND FATE OF ATMOSPHERIC CARBON MONOXIDE

1. Background Levels and Estimated Mean Lifetime of Carbon Monoxide

The amount of CO measurable in relatively unpolluted ("clean") air is small. Junge has estimated the background level of CO in the lower atmosphere to be in the range of 0.01 to 0.2 mg/m^3 (0.01 to 0.2 ppm).[34] Studies of background levels of CO using solar spectral techniques at Mt. Wilson, California; Ottawa, Canada; Jungfraujoch, Switzerland; and Columbus, Ohio, confirmed that such levels average about 0.1 mg/m^3 (0.1 ppm).[35-37] There appears to be no significant variation in such levels with geographical locations.[37] Robbins et al.,[38] using an experimental, continuous-measurement HgO method sensitive in parts per billion (ppb), have recently determined that North Pacific marine air mass concentrations may contain as little as 0.029 mg/m^3 (0.025 ppm) and the clean (nonurban) air mass over continental California contains 0.06 to 1.2 mg/m^3 (0.05 to 1.0 ppm). These investigators have also determined, on the basis of a 12-day sample, that typical background levels of CO at Inge Lehmann Station in northern Greenland range from 0.06 to 0.75 mg/m^3 (0.05 to 0.65 ppm).[39] The variability of CO in nonpolluted areas appears to be a characteristic of the air mass in transit and reflects its prior history. Robinson and Robbins estimate that arctic air masses passing over Greenland have CO concentrations of between 0.11 and 0.23 mg/m^3 (0.10 and 0.20 ppm) and that concentrations of 0.6 to 1.2 mg/m^3 (0.5 to 1.0 ppm) can occur when the air mass has recently traversed a heavily populated area.[39] Measurements at Point Barrow, Alaska, gave clear air CO levels, ranging from 0.063 to 0.299 mg/m^3 (0.055 to 0.260 ppm) and averaging 0.104 mg/m^3 (0.90 ppm).[40]

The exact turnover time of CO in the atmosphere is not known with certainty. A recent estimate, derived from radioactive measurements, of the residence time of CO in the lower atmosphere has a lower limit of 0.1 year.[41] Another estimate based on different technique is 3 years.[34] (The published estimate of 0.3 year given in reference 34 is based on a miscalculation)[42] Robbins et al. estimate a mean residence time of about 5 years, and have tentatively concluded that the background levels of CO are not rising significantly at the persent time.[38]

The previously discussed relative inertness of CO in reactions with the normal gaseous atmospheric constituents and its photon transparency[43] effectively eliminate the possibility of chemical reactions as a mechanism for CO removal in the lower atmosphere with the possible exception of the still speculative reaction with the hydroxyl radical.

In spite of the above, calculations have shown that in the absence of removal processes, the estimated world-wide emissions of CO from technological sources (estimated to be on the order of 1.8 to 2.1 x 10^{11} kg or 198 to 231 million tons per year[13,40]) would be sufficient to raise the atmospheric background concentration of CO by 0.03 mg/m^3 (0.03 ppm) per year creating a current background level of 1 mg/m^3 (1 ppm).[9,38,44] It is therefore postulated that some "sink" or removal process for atmospheric CO exists.

2. Possible Processes for Carbon Monoxide Removal

The following discussion represents a review of possible CO removal processes. Some of the CO "sinks" discussed below are highly speculative, however; in fact, they may actually contribute CO rather than remove it from the atmosphere.

a. *Atmospheric Migration (Upper Atmospheric Sink).*

Conceivably CO in the lower atmosphere may eventually migrate by atmospheric mixing to a potential sink in the upper atmosphere, where it is oxidized to CO_2 in the presence of high-intensity ultraviolet solar radiation. A recent laboratory study by Harteck and Reeves[45] confirmed that CO, in the presence of NO_2 or other absorbing molecules, when subjected to high-intensity, ultraviolet radiation in an evacuated chamber, was oxidized to CO_2.

b. *Biological Removal (Terrestrial and Marine Biosphere Sink).*

Another possible removal agent of atmospheric CO is the presence, in significant numbers, of plants and microorganisms that can metabolize CO. The earth's surface is a possible vector for the removal of CO from the atmosphere. Carbon monoxide in contact with the soil may be oxidized to CO_2 and converted to methane (CH_4) by common specific anaerobic methane-producing soil microorganisms, *Methanosarcina barkerii* and *Methanobacterium formicum,* in the presence of moisture.

This action has been demonstrated in the laboratory by Schnellen,[46] who showed that pure cultures of these bacteria convert CO into methane. Schnellen has found that *Ms. barkerii* is capable of converting CO to CH_4 according to the equation:

$$4\,CO + 2\,H_2O \rightarrow CH_4 + 3\,CO_2 \qquad (7)$$

Stephenson,[47] however, indicates that CO, in the absence of H_2, reacts with water in these bacteria in two stages as follows:

$$4\,CO + 4\,H_2O \rightarrow 4\,CO_2 + H_2 \qquad (8)$$

and

$$CO_2 + 4\,H_2 \rightarrow CH_4 + 2\,H_2O. \qquad (9)$$

In the presence of H_2, these bacteria convert CO directly into methane and water:

$$CO + 3\,H_2 \rightarrow CH_4 + H_2O. \qquad (10)$$

An aerobic soil bacterium, *Bacillus oligocarbophilus (Carboxydomonas oligocarbophila),* found in and isolated from arable soil, has also been demonstrated to oxidize CO to CO_2. When cultivated on simple organic media free from other carbon sources, this organism oxidizes CO to CO_2, which is then utilized as a source of energy.[48] Another bacterium, *Clostridium welchii,* when grown in the presence of CO, has been reported to produce lactic acid as a fermentation product.[49]

Although these soil bacteria utilize CO in their fermentation or metabolic processes, it is difficult to estimate global destruction rates of CO on the basis of such laboratory experiments.

Within the biosphere, the process of plant respiration may serve as a potential removal process; but this concept has not been firmly established, even though it is recognized that plants are scavengers for a wide variety of atmospheric materials. Chapter 7 of this document treats this subject in greater detail.

c. *Biochemical Removal (Biochemical Sink).*

A potential biochemical removal process for CO is the binding of CO to the porphyrin-type compounds that are widely distributed in plants and animals. In particular, the heme compounds such as hemoglobin, which are analogous to porphyrin compounds found in plants are known to bind CO. It must be noted, however, that practically all of the CO absorbed by the heme compounds found in man and animals is eventually discharged from the blood, and only a small fraction is retained.[50] This type of process in vegetation may have an important potential for scavenging atmospheric CO.Permanent removal from the environment, however, would depend on whether CO subsequently enters into some reaction process to form CO_2 when the porphyrin compound is degraded.

d. *Absorption in Oceans (Oceanic Sink).*

While absorption in the world's oceans is a recognized sink process for atmospheric CO_2, there is no evidence at present that the oceans are a sink for CO because no process or reaction that would remove CO has been discovered.[1,14] The solubility of CO at 1 atmosphere (atm) pressure in sea water ranges from about 17 to 32 milliliters CO (0°C, 1 atm)/liter water over a water temperature and chlorinity range of -2° to 30°C and 15 to 21 grams of chlorine per kilogram of water, respectively.[51] This solubility is too low for the oceans to accumulate CO or for precipitation washout to be an effective scavenging agent. An apparent daily cycle for CO concentrations over ocean areas seems to indicate some involvement of the ocean in the fate of CO.[34] The high CO concentrations in some marine plants[14] may also be indicative of some complex system in the ocean involving CO.

Swinnerton et al. simultaneously sampled the CO content of the air and the surface waters at 29 different points along the path of an oceanographic cruise between Washington, D.C., and Puerto Rico.[52] These investigators found that the measured concentrations of CO in the water exceeded by 7 to 90 times the concentrations of CO theoretically expected to be present based on solubility calculations. Apparently, man-made pollution is not the principal source of CO in sea water, since the highest ratios were found in the open ocean. The ocean, therefore, may be a source rather than a sink for atmospheric CO, as discussed previously.

e. *Adsorption on Surfaces.*

Kummler et al. indicate that the gas-phase oxidation of CO by nitrous oxide (N_2O), considered too slow to be of importance in the atmosphere, is catalyzed in the presence of certain surfaces (such as charcoal, carbon black, and glass) at 300°C and above.[53] These investigators have extrapolated these reported high-temperature reaction rates to 27°C and consider that such a catalytic reaction is feasible at ambient temperatures. This conclusion is supported by laboratory studies of Gardner and Petrucci, where the chemisorption of CO on metallic films (such as copper, cobalt, and nickel oxides) at room temperatures have been measured by infrared spectroscopy.[54]

The necessary data for evaluation of the catalytic efficiency of common surfaces such as metals, soil, and atmospheric particles are presently unavailable; therefore, the possibility of such surfaces serving as a sink by adsorption of atmospheric CO is uncertain.

F. SUMMARY

Carbon monoxide constitutes the largest single fraction of the pollutants found in urban atmospheres. It is produced primarily by the incomplete combustion of organic materials used as fuels for transportation and in the heating of buildings; it also results from industrial processes, refuse burning, and agricultural burning. Several natural sources of CO of both biological and nonbiological origin have also been identified, but their contributions to urban atmospheric concentrations are thought to be small. Background levels of CO (resulting from natural and technological sources) found in relatively unpolluted air range from 0.029 to 1.15 mg/m^3 (0.025 to 1.0 ppm).

Carbon monoxide is colorless, tasteless, and odorless; although flammable, it does not support combustion. Oxidation reactions with both oxygen and water vapor are known to involve CO in the lower atmosphere, but the rate of these reactions is very slow.

Worldwide emissions of CO from technological sources have been estimated to be more than 1.8×10^{11} kg (200 million tons) annually. In the absence of any removal processes, this large tonnage would be sufficient to raise the background level of CO by 0.03 mg/m^3 (0.03 ppm) per year; yet these background levels do not appear to be rising. The mean residence time of atmospheric CO has been estimated to be between 1 month and 5 years.

Several "sinks", or removal processes, have been postulated in an attempt to explain the apparent constancy of the background CO levels. These processes include: the migration of CO to the upper atmosphere, where oxidation to CO_2 may subsequently take place; the removal of CO by the terrestrial and marine biospheres, through processes such as the metabolic conversion of CO to CO_2 and methane by soil microorganisms; the binding of CO to porphyrin compounds in plants and animals, with subsequent oxidation of the CO to CO_2; an interaction between CO and ocean water, or some agent in ocean water; and the adsorption and subsequent oxidation of CO on various surfaces. Although the biosphere provides several potential mechanisms involving both land and marine plant and animal communities, the precise mechanism of removal of CO from the atmosphere cannot at present be identified with any certainty. In fact, some of the CO sinks discussed above are highly speculative and may actually contribute rather than remove CO from the atmosphere.

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CHAPTER 3.

PRINCIPLES OF FORMATION AND CONTROL OF CARBON MONOXIDE

A. INTRODUCTION

Carbon monoxide formation results directly from the incomplete combustion of a gaseous, liquid, or solid carbon-containing fuel; therefore, the CO found in urban air generally has its origin in one of the many combustion processes associated with man's day-to-day activities, industry, and commerce. It is the purpose of this chapter to discuss the general mechanisms of combustion leading to the formation of CO and their specific involvement in CO formation in mobile and stationary sources.

A more detailed discussion of the information presented in this chapter may be found in AP-65, *Control Techniques for Carbon Monoxide Emissions from Stationary Sources*, and AP-66, *Control Techniques for Carbon Monoxide, Nitrogen Oxide, and Hydrocarbon Emissions from Mobile Sources.*

B. FORMATION OF CARBON MONOXIDE BY COMBUSTION

1. General Combustion Processes

Incomplete combustion of carbon or carbon-containing compounds creates varying amounts of CO. The chemical and physical processes that occur during this combustion are complex, because they depend not only on the type of carbon compound reacting with oxygen, but also on the conditions existing in the combustion chamber. Despite the complexity of the combustion process, certain general principles regarding the formation of CO from the combustion of hydrocarbon fuels are widely accepted.

Gaseous or liquid hydrocarbon fuel reacts with molecular oxygen in a chain of reactions that result in CO. Carbon monoxide then reacts with hydroxyl radicals to form carbon dioxide (CO_2). This second reaction is approximately ten times slower than the first. In coal combustion, the reaction of carbon and oxygen to form CO is also one of the primary reactions, and a large fraction of carbon atoms go through the monoxide form. Again the reaction of monoxide to dioxide is much slower.

Consideration of this mechanism leads to four basic variables that control the concentration of CO in all combustion of hydrocarbon gases. These are (1) oxygen concentration, (2) flame temperature, (3) gas residence time at high temperature, and (4) combustion chamber turbulence. Oxygen concentration affects the formation of both CO and CO_2 because oxygen is required in the initial reactions with the fuel molecule and in the formation of the hydroxyl radical. As the availability of oxygen increases, more complete conversion of monoxide to dioxide results. Flame temperature affects both the formation of monoxide and the conversion of monoxide to dioxide because both reaction rates increase exponentially with increasing temperature. The conversion of CO to CO_2 is also enhanced by longer residence time because this is a relatively slow reaction compared to CO formation. Increasing combustion-gas turbulence increases the actual reaction rates by by-passing the relatively slower gaseous diffusion mixing process.

2. Internal Combustion Engines

The two factors that effectively determine total CO emissions from internal combustion engines are the concentration of CO in the exhaust and the exhaust volume. The exhaust concentration depends mainly on the air-to-fuel (A/F) ratio entering the combustion cylinder; the exhaust volume depends on the power output.

Exhaust concentrations of CO increase with lower (richer) A/F ratios, decrease with higher (leaner) A/F ratios, but remain relatively constant with ratios above the stoichiometric ratio of about 14.5 to 1.[1] The behavior of gasoline automobile engines before and after the imposition of pollutant control measures differs considerably. Depending on the mode of driving, the average precontrol engine operates at A/F ratios ranging from about 11 to a point slightly above the stoichiometric ratio. During the idling mode, at low speeds with light load (such as low-speed cruise), during the full-throttle mode until speed picks up, and during deceleration, the A/F ratio is low in precontrol cars and CO emissions are high. At higher speed cruise and during moderate acceleration, the reverse is true. Cars with exhaust controls generally remain much closer to stoichiometric A/F ratios in all modes, and thereby the CO emissions are kept lower. The relationship between CO concentration in exhaust and the A/F ratio is shown in Figure 3-1.

The exhaust flow rate increases with increasing engine power output. During idle the flow is minimum; during full throttle it is maximum. At cruise engine conditions (i.e., constant engine speed and power output) the exhaust flow remains constant. It increases during engine acceleration.

Correlations between total emissions of CO in pounds per vehicle mile and average route speed (discussed in greater detail in Chapter 4) show a decrease in emissions with increasing average speed. The greater emissions per mile during the low-speed conditions (below 20 miles per hour) are due to an increase in the frequency of the acceleration, deceleration, and idle stages of the driving cycle encountered in heavy traffic.

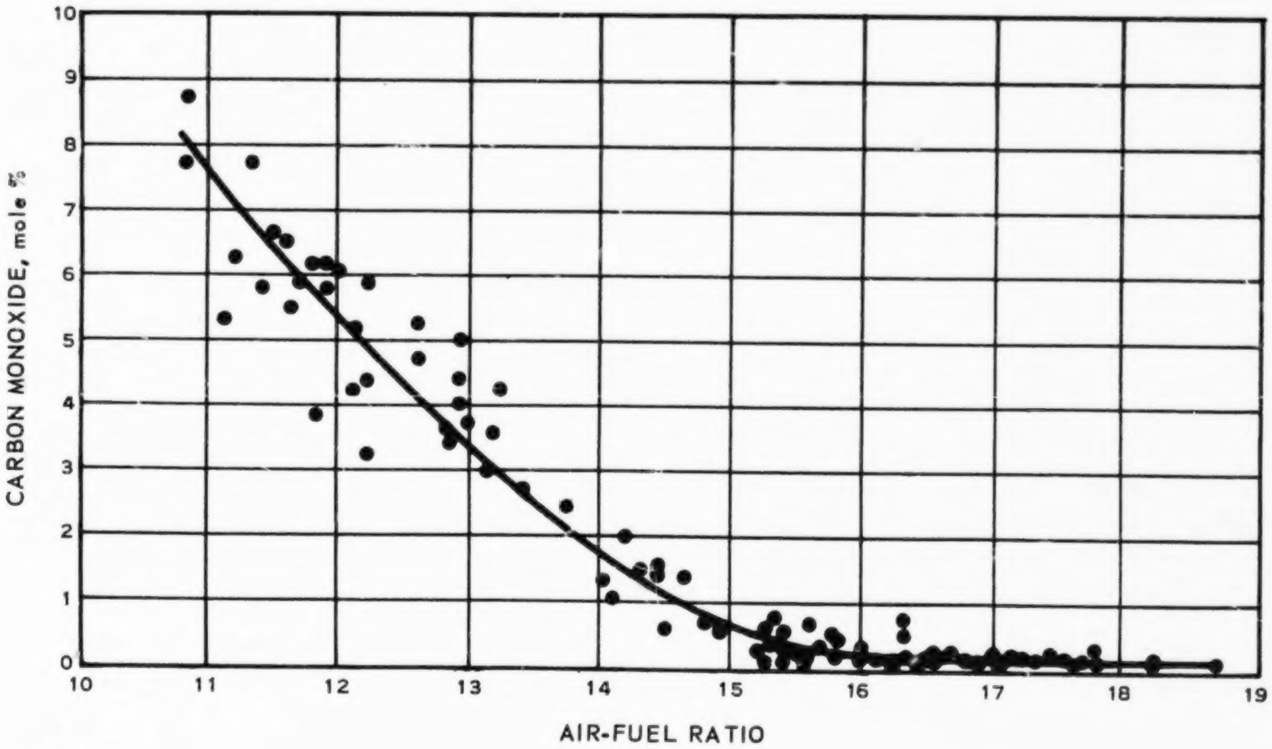

Figure 3-1. Effect of air-fuel ratio on exhaust gas carbon monoxide concentrations from three test engines.[1]

3. Stationary Combustion Sources

In stationary combustion systems, the concentration of CO is lowest near the stoichiometric ratio of air to fuel. At lower than stoichiometric A/F ratios, high CO concentrations reflect the relatively low oxygen concentration and the possibility of poor reactant mixing from low turbulence. These two factors can increase emissions even though flame temperatures and residence time are high. At higher than stoichiometric A/F ratios, increased CO emissions result from decreased flame temperatures and shorter residence times. These two factors control even though oxygen concentrations and turbulence increase. Minimal CO emissions and maximum thermal efficiency therefore require combustor designs that provide high turbulence, sufficient residence time, high temperatures, and near stoichiometric A/F ratios. Combustor design dictates the minimum CO emission that can be achieved, and operating practice dictates the actual approach to that minimum.

C. SUMMARY

Carbon monoxide arises predominantly from incomplete or inefficient combustion. If any of the four variables that control this process are low, CO may be high. These variables are: (1) oxygen concentration, (2) flame temperature, (3) gas residence time at high temperature, and (4) combustion chamber turbulence. In the internal combustion engine the air/fuel ratio, corresponding to variable (1) above, is controlling for CO concentration in the exhaust, whereas the total volume of exhaust relates to power output. In stationary sources, combustor design and operation determine the CO emissions.

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CHAPTER 4.

ESTIMATION OF CARBON MONOXIDE EMISSIONS

A. INTRODUCTION

The potential for CO emissions exists everywhere man uses his ancient ally, fire. Since combustion takes such a multitude of forms, the task of evaluating the relative importance of different CO sources requires considerable variety in methods of estimation. Of the numerous source categories of CO, fuel combustion in mobile sources utilizing the internal combustion engine is the principal source category of CO in the United States. Miscellaneous combustion sources, principally forest fires, and industrial process sources are the second and third largest categories of CO emissions. Disposal of solid wastes, either by open burning or incineration, and stationary fuel combustion are the fourth and fifth largest categories, respectively.

A more detailed discussion of the information presented in this chapter may be found in AP-65, *Control Techniques for Carbon Monoxide from Stationary Sources,* and AP-66, *Control Techniques for Carbon Monoxide, Nitrogen Oxide and Hydrocarbon Emissions from Mobile Sources.*

B. RECENT CARBON MONOXIDE EMISSION LEVELS

1. National Emission Levels

An estimated 92 x 10^9 kilograms (102 million tons) of CO was emitted in the United States in 1968 – 50 percent by weight of all major air pollutant emissions for that year.[1] Contributions by source categories to the estimated national emission of CO are presented in Tables 4–1 and 4–2.

CO emission estimates were derived by the use of emission factors and activity levels. The emission factors were developed from source testing data, material balances, and theoretical calculations; the activity levels were based on such quantities as vehicle miles of travel, fuel consumption, airplane landing and take-off cycles, and industrial process production.

2. Regional Emission Levels

Emission surveys have been conducted in various cities in the United States in order to determine the nature and amount of air pollutants emitted in these communities. Comparative emission data from recent emission inventories of selected metropolitan areas are presented in Table 4–3 for the years 1967 through 1968. These inventories are based on a modified rapid survey technique using grid coordinates. Limitations of the rapid survey technique are discussed by Ozolins.[2] The relative contributions from different emission sources to the total CO emissions vary within each surveyed area. This variability is shown for 11 selected cities in Figure 4-1. In all areas, the major source of CO is transportation, which includes emissions from motor vehicles, aircraft, trains, and ships.

Table 4–3 includes emission data from areas constituting 58 percent of the 1968 urban population of the United States. These emission estimates were obtained by using specific regional data obtained by government surveys. In all but two of the 26 cities in the table, CO emissions are greater than those of any other pollutant reported.

C. EMISSIONS AND EMISSION FACTORS BY SOURCE TYPE

1. Mobile Combustion Sources

a. Motor Vehicles

The largest single source of CO (more than 58 percent of the national total) is the exhaust of motor vehicles, both gasoline- and

Table 4–1. CARBON MONOXIDE EMISSION ESTIMATES BY SOURCE CATEGORY–1968[a]

Source	CO emissions, 10^6 tons/yr			Percent of total		
Transportation	**63.8**			**62.8**		
Motor vehicles		59.2			58.2	
Gasoline			*59.0*			*58.0*
Diesel			*0.2*			*0.2*
Aircraft		2.4			2.4	
Vessels		0.3			0.3	
Railroads		0.1			0.1	
Other non-highway use of motor fuels		1.8			1.8	
Fuel combustion in stationary sources	**1.9**			**1.9**		
Coal		0.8			0.8	
Fuel oil		0.1			0.1	
Natural gas		N			N	
Wood		1.0			1.0	
Industrial processes	**11.2**			**11.0**		
Solid waste disposal	**7.8**			**7.7**		
Miscellaneous	**16.9**			**16.6**		
Man made		9.7			9.5	
Forest fires		7.2			7.1	
Total	**101.6**			**100.0**		

N = Negligible.

[a] These emission estimates are subject to revision as more refined information becomes available.

diesel-powered. Other vehicle emissions, such as hydrocarbons, may come from the fuel tank, crankcase, or carburetor, as well as from the exhaust, but of these only the exhaust is a significant source of CO.[3-7]

The quantity of emissions from a single vehicle is not large. They vary in automobiles by more than an order of magnitude from the lowest emitters among new vehicles with control systems to the highest emitters among uncontrolled vehicles, but are usually in the range of 1 to 4 percent by volume in the exhaust over a complete representative driving cycle. The national average in 1968 was about 33 grams per kilometer (53 g/mi), but since 1.63 x 10^{12} vehicle-kilometers (1015 billion vehicle-miles) were traveled, the total national emissions reached the substantial value of 5.4 x 10^{10} kilograms (5.9 x 10^7 tons) of CO.

Table 4–2. CARBON MONOXIDE EMISSION ESTIMATES - 1968

Source	Emissions, 10^6 tons/yr	Emission factor
Mobile combustion sources		
Motor vehicles		
Light-duty vehicles - urban	35.6	Based on method described in text
- rural	12.8	
Heavy-duty vehicles		
Class II (6,000 - 10,000 lb[a]) - urban	1.7	
- rural	0.9	
Class III (10,000 - 19,500 lb[a]) - urban	1.4	
- rural	0.8	
Class IV (>19,500 lb[a]) - urban	3.0	
- rural	2.8	
Diesel	0.2	
Aircraft		
FAA Controlled	1.1[b]	Based on LTO cycle - see text
Military	1.3[b]	
Railroad	0.1	Distillate fuel oil: 60 lb CO/10^3 gal.
Vessels	0.3	Distillate fuel oil: 60 lb CO/10^3 gal. gasoline: 2300 lb CO/10^3 gal.
Non highway fuel uses	1.8	
Fuel combustion in stationary sources		
Coal		
Electrical power	0.1	0.5 lb CO/ton
Industrial	0.2[c]	3.0 lb CO/ton
Domestic and commercial	0.5	50.0 lb CO/ton
Fuel oil		
Domestic, industrial, and miscellaneous	0.1	84.0 lb CO/10^3 bbl
Electric power	N	1.7 lb CO/10^3 bbl
Wood	1.0	45 lb CO/ton
Industrial processes		
Foundries		
Controlled (with afterburners)	0.2	10 lb CO/ton of charge
Uncontrolled	3.1	250 lb CO/ton of charge
Petroleum Refineries		
Fluid catalytic crackers	2.0	13.7 lb CO/bbl of fresh feed
Fluid coking	0.2	30 lb CO/bbl of fresh feed
Moving-bed catalytic crackers	0.2	3.8 lb CO/bbl of fresh feed
Kraft pulp mills	2.6	215 lb CO/ton of product
Carbon black		
Furnace	0.30	560 lb CO/ton of product
Channel	0.05[d]	
Thermal	0.01	47 lb CO/ton of product
Steel mills		
Beehive coke ovens	0.02	4.5% of exhaust gas by volume
Basic oxygen furnaces	0.1	3.2% of exhaust gas by volume
Sintering	2.4	500 ft^3/ton
Formaldehyde	0.03	100 lb CO/ton of product

TABLE 4–2. (Continued) CARBON MONOXIDE ESTIMATES - 1968

Source	Emissions, 10^6 tons/yr	Emission factor
Solid waste combustion		
Incineration		
Municipal	0.01	1 lb CO/ton
On site	0.8	27 lb CO/ton
Open burning		
Municipal	1.7	85 lb CO/ton
Industrial	0.9	85 lb CO/ton
Commercial, backyard, etc.	0.8	85 lb CO/ton
Metal conical burners	3.6	260 lb CO/ton
Miscellaneous combustion		
Building fires	0.2	45 lb CO/ton
Forest fires	7.2	60 lb CO/ton
Coal banks	1.2	50 lb CO/ton
Agriculture	8.3	60 lb CO/ton

N = Negligible.
[a]Gross vehicle weight.
[b]Under 3,000 feet.
[c]Does not include 96,400 tons from coke plants.
[d]Gross estimate.

The annual CO emission estimates for motor vehicles presented in Table 4–1 were derived from a method of analysis that combines actual on-the-road exhaust sampling data, with simulated driving-cycle data. This method incorporates emission rates for four classes of vehicles (one class for passenger cars plus light-duty trucks, and three classes for heavy-duty trucks, including diesel trucks). These emission rates are applied to national vehicle activity data with consideration of vehicle operating characteristics, including urban-rural vehicle speed, vehicle age, and vehicle deterioration. Three levels of controls are represented: (1) 1967 and earlier, (2) 1968-69, and (3) 1970 and later. The past and projected trends in CO emissions from motor vehicles is depicted in Figure 4–2.

Exhaust emissions from motor vehicles have been expressed in the literature either in terms of concentrations in ppm of the contaminants emitted from the tailpipe or in terms of weight in grams or pounds of contaminants per vehicle-mile traveled.[3-9] The latter method of expressing emissions is considered to be more representative and preferable since it is consistent with data on average traffic volume for major metropolitan areas (vehicle-miles traveled), and it can be related directly to engine power demands of the vehicle over various types of routes.[9] Exhaust emissions expressed as ppm can be converted to pounds per mile if the exhaust volume per unit time and the vehicle speed are known.

The data for determination of motor vehicle national emissions based on the road-factor method are derived from recent studies. These studies of emission data, based on road tests of a number of vehicles under average traffic conditions, indicate that the average speed of a vehicle is a measure that provides an adequate index of emissions over a specific route pattern.[5,9,10] This parameter, called "average route speed," appears to reflect the engine power demand and consequent pollutant emissions that are associated with the acceleration, deceleration, cruise, and idle driving modes imposed by the

Table 4–3. SUMMARY OF TOTAL EMISSIONS FROM METROPOLITAN AREAS THROUGHOUT UNITED STATES - 1967–1968

Standard metropolitan statistical area	Population	Area, mi^2	Emissions, 10^3 tons/yr				
			SO_x	Particulate	HC	NO_x	CO
N.Y. - N.J.[a]	15,420,000	6,930	1,590	231	N.A.	N.A.	5,297
Chicago[b]	7,500,000	4,660	1,780	586	N.A.	N.A.	2,726
Los Angeles[c]	7,070,000	41,000	168	103	1,268	471	4,997
Philadelphia[d]	5,550,000	4,590	1,168	241	468	406	2,691
San Francisco[e]	4,500,000	7,000	157	77	788	188	2,520
Detroit[f]	4,090,000	2,680	786	241	481	300	1,896
Cleveland[g]	3,030,000	3,500	819	304	N.A.	N.A.	1,384
Washington, D.C.	2,720,000	2,270	247	35	310	135	1,259
Boston	2,700,000	1,280	424	82	87	168	921
Pittsburgh	2,520,000	3,050	934	387	95	267	915
St. Louis[h]	2,410,000	4,500	662	176	326	181	1,643
Hartford and New Haven[i]	2,290,000	2,650	337	56	123	134	846
Seattle and Tacoma[j]	2,010,000	15,000	255	33	165	74	907
Houston and Galveston[k]	2,000,000	7,800	144	156	292	213	1,100
Milwaukee[l]	1,730,000	2,630	243	100	83	111	619
Minneapolis-St. Paul[m]	1,660,000	2,830	215	46	N.A.	N.A.	960
Cincinnati[n]	1,660,000	2,620	428	123	55	130	537
Buffalo	1,320,000	1,470	410	140	93	130	470
Denver[o]	1,230,000	10,300	31	33	N.A.	N.A.	616
Kansas City[p]	1,230,000	3,200	125	60	233	N.A.	744
Providence[q]	1,200,000	1,000	118	23	54	64	435
Indianapolis	1,050,000	3,080	164	78	74	69	757
Dayton[r]	880,000	2,310	108	94	64	62	367
Louisville[s]	840,000	1,390	303	128	46	44	305
Birmingham[t]	750,000	1,120	34	205	64	26	253
Steubenville[u]	370,000	1,530	638	155	N.A.	N.A.	152

N.A. = not available.,

[a] Includes New York S.M.S.A. less Suffolk County, Jersey City S.M.S.A., Patterson-Clifton-Passaic S.M.S.A., and Somerset, Middlesex and Monmouth Counties, N.J. and Fairfield County, Conn.

[b] Includes Chicago and Gary-Hammond-East Chicago S.M.S.A.'s.

[c] Includes Los Angeles-Long Beach, Oxnard-Ventura, Anaheim-Santa Ana-Garden Grove, San Bernardino-Riverside-Ontario, and San Diego S.M.S.A.'s.

[d] Includes Philadelphia S.M.S.A., Trenton S.M.S.A. and Wilmington S.M.S.A. less Cecil County.

[e] Includes San Francisco-Oakland S.M.S.A., San Jose S.M.S.A., Vallejo-Napa S.M.S.A. and Sonoma County.

[f] Plus St. Clair County.

[g] Includes Cleveland, Lorain-Elyria, Akron, and Canton S.M.S.A.'s.

[h] Plus Monroe County, Ill.

[i] Plus Hampden County, less Tolland County.

[j] Plus Skagit, Whatcom, Thurston, Mason, Kitsap, Jefferson and Clallam Counties.

[k] Plus Chambers and Waller Counties.

[l] Includes Milwaukee S.M.S.A., Racine S.M.S.A., Kenosha S.M.S.A., and Walworth County.

[m] Plus Carver and Scott Counties.

[n] Plus Butler County.

[o] Plus Larimer and Weld Counties.

[p] Plus Leavenworth County, Ky.

[q] Includes Providence-Pawtucket-Warwick S.M.S.A., Falls River S.M.S.A., New Bedford S.M.S.A., and Newport County.

[r] Plus Darke and Sheby Counties.

[s] Plus Oldham and Bullitt Counties.

[t] Less Shelby and Walker Counties.

[u] Includes Steubenville-Weirton and Wheeling S.M.S.A.'s.

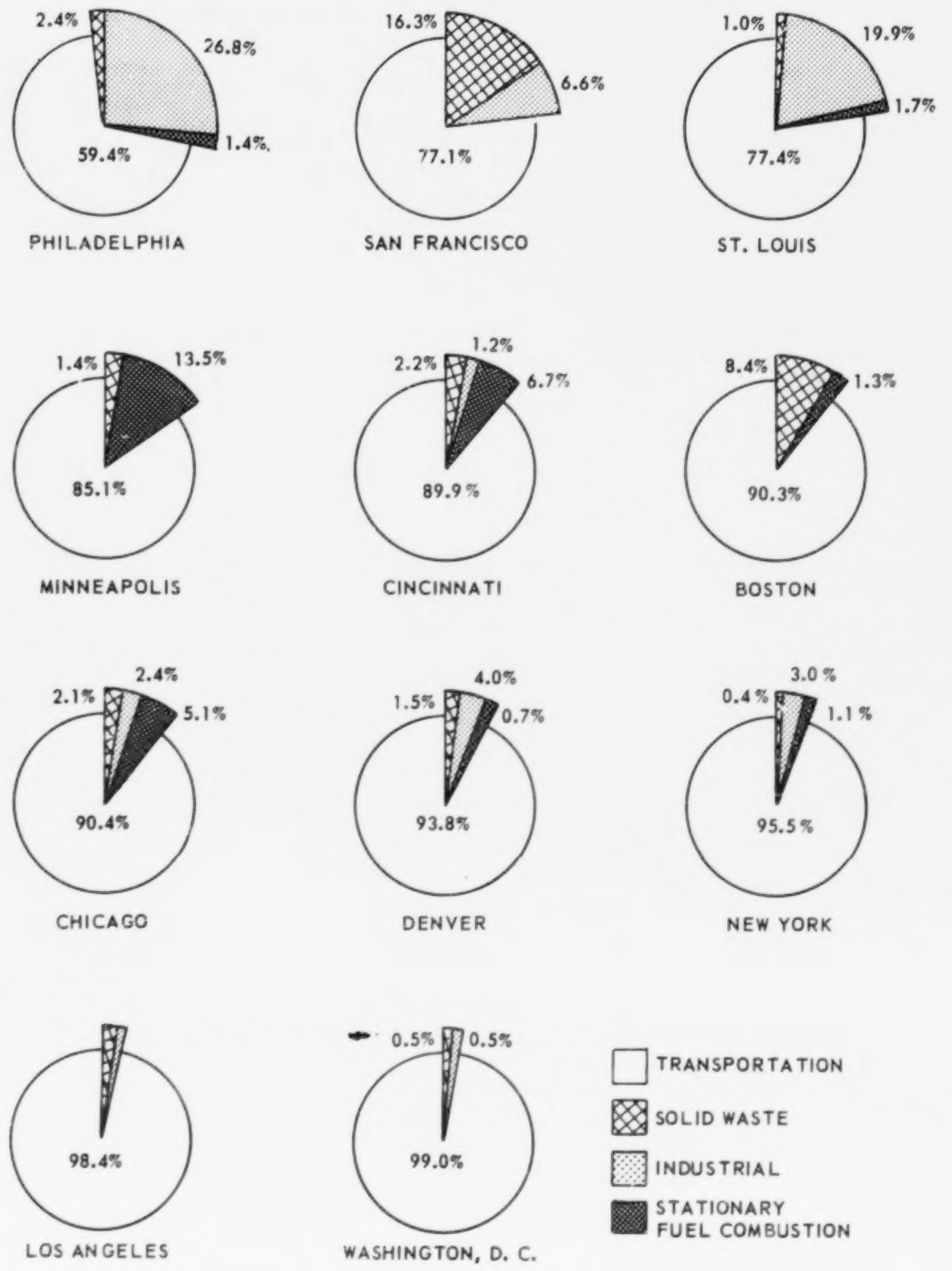

Figure 4-1. Carbon monoxide emissions by source category for various U.S. metropolitan areas in 1968.

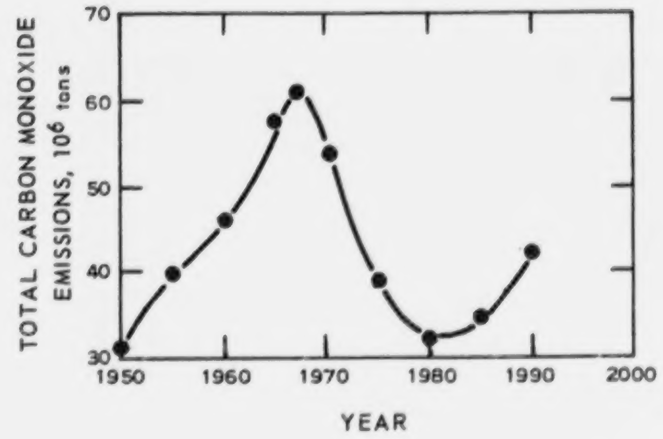

Figure 4-2. Forecast of total carbon monoxide emissions from motor vehicles.

many driving variables such as route, topography, traffic density, climate, and altitude.

Evaluation of auto exhaust data by Rose et al.[9] indicated that an empirical relationship between speed and CO emission level in pounds can best be satisfied or expressed by an inverse power function of the average route speed:

$$Y = AX^{-b}$$

where: Y = weight of CO emitted
X = *average route speed*
A, b are constants.

From this study, and also the study of McMichael and Rose,[10] it has been established statistically that average route speed is related more nearly to weight of emissions per mile rather than to exhaust concentration. When CO emissions from 40 randomly selected test vehicles in Cincinnati and Los Angeles were expressed in ppm and regressed on vehicle speed, the correlation coefficient was found to be 0.446 (0.31 to 0.58 at 95 percent confidence). For the same test, when CO emissions were expressed as pounds of CO per mile and regressed on vehicle speed, the correlation coefficient was found to be 0.613 (0.49 to 0.71 at 95 percent confidence). See Figure 4–3. Further statistical analysis with individual vehicles showed that most of the observed variance was due to differences among vehicles rather than to a poor correlation between CO weight emissions and route speed (Figure 4–4).

Carbon monoxide emissions are proportionately greater during the low-speed conditions below 20 miles per hour because of an increase in frequency of the acceleration, deceleration, and idle stages of the driving cycle representative of heavier traffic.[9] The same relationship between mass emissions and average route speed holds for the low air-to-fuel (A/F) ratio operation encountered during high-altitude driving conditions.[10]

The significance of this relationship between vehicle speed and CO emissions has not

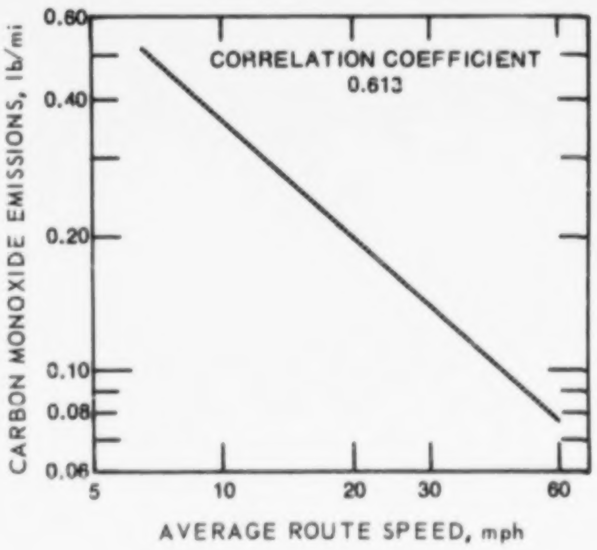

Figure 4-3. Effect of average route speed on carbon monoxide emission by weight.[10]

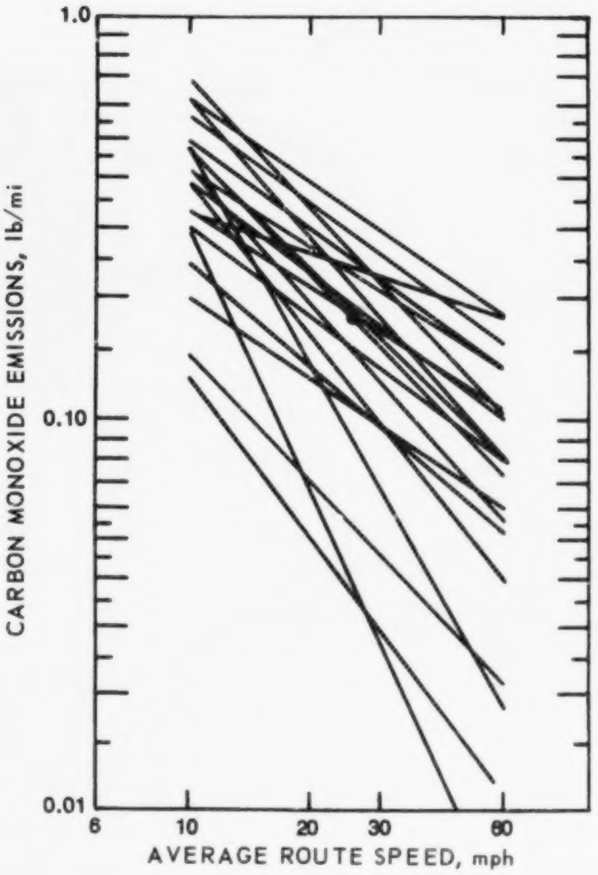

Figure 4-4. Carbon monoxide emissions by individual vehicles, Los Angeles.[9]

been fully exploited. Since emissions of CO (and, incidentally, hydrocarbons) are lower for higher average route speeds, proper community and highway planning should recognize that higher speed movement of traffic within the urban area can effectively reduce the gross emissions from the exhaust of the automobile to the lower atmosphere. For example, an increase in average urban route speed from 25 to 35 mph can result in a reduction of roughly one-fourth in the mass of CO emitted to the atmosphere. See Figure 4–3. The implications of such emission control by means of urban planning are covered in greater detail in AP-66, *Control Techniques for Carbon Monoxide, Nitrogen Oxide, and Hydrocarbon Emissions from Mobile Sources.*

Gasoline engines produce much more CO per unit of power output than do diesel engines primarily because of the lower A/F ratio, and the resulting less complete combustion by gasoline-powered vehicles.[3-7] Carbureted engines, such as are generally found in passenger vehicles, operate with a deficiency of combustion air under some conditions; whereas the diesel engine normally operates with combustion air in substantial excess of stoichiometric requirements.

b. *Aircraft*

The contribution from aircraft to the total National atmospheric CO pollution burden is at present only slightly more than 2 percent. This contribution is expected to increase, however, in both magnitude and in relative percentage. A projection of the potential rise in total CO emissions from the civil aircraft population between 1967 and 1979 has been estimated to be 59 percent over the base figure of 0.84 x 10^9 kilograms (0.93 million tons) calculated for 1967.[11] Although at this time the contribution of aircraft to total CO emissions is small, atmospheric concentrations of CO at and near airports may be creating a localized problem.

The civil aircraft population is the source of approximately half of the CO emissions attributed to aircraft; military aircraft contribute the remaining half. Civil aircraft may be classified as: (1) general aviation aircraft (> 99 percent piston powered) and (2) commercial carriers (> 85 percent turbine powered). Commercial carriers, while constituting only about 2 percent of the civil aircraft population, nevertheless account for 20 percent of the activity at civilian aircraft terminals. Civil aircraft at terminals not controlled by the Federal Aviation Administration represent a negligible addition to total aircraft emissions.

In the calculation of aircraft emissions, the general practice is to include only those emissions below an arbitrarily chosen height of 3000 to 3500 feet. The pollution emitted at higher altitudes cannot be considered in the same light as that emitted at or near ground level. The emission factors for aircraft presented in this chapter were estimated from the results of a study[11] and report to Congress and were based on actual sampling data.

Emissions at evaluations below 3000 feet were estimated on the basis of a five-mode landing-take-off (LTO) cycle, which included approach, landing, taxiing, takeoff, and climbout. Though only about 20 percent of the total aircraft fuel is consumed during the LTO cycle, it accounts for approximately 83 percent of the total CO emitted during an entire trip (LTO cycle plus cruise mode).[11]

Emission factors were derived and expressed as weight of CO emitted per unit time by a particular class of aircraft operating in a particular mode. Knowledge of the time-frequency distribution by class and mode allowed calculation of the figure for total aircraft CO emissions presented in Tables 4–1 and 4–2.

c. *Other Non-Highway Mobile Sources*

According to the Bureau of Roads and the Bureau of Mines, the total non-highway use of motor fuels, excluding aircraft, amounted to 8.20 billion gallons for 1966.[12-14] This total represents the consumption of gasoline and diesel fuel by trains, ships, agricultural machinery, commercial equipment, and construction machinery. Trains and ships also consumed distillate fuel oil, residual fuel oil, and coal.

The emissions of CO were calculated using emission factors of 2,300 pounds of CO per 1000 gallons of gasoline and 60 pounds of CO per 1000 gallons of the other liquid fuels. The emission estimates are presented in Tables 4–1 and 4–2.

2. Carbon Monoxide from Combustion for Power and Heat

The combustion of coal, fuel oil, natural gas, and wood to produce power and heat also produces a small, but significant, quantity of CO when viewed on a national scale. On a smaller scale, other fuels such as bottled gas and kerosine are used for miscellaneous heating purposes. By far the largest percentage of CO emissions in each fuel category may be attributed to residential, commercial, institutional, and light industrial burning. This is brought about by the relatively inefficient nature of combustion associated with these facilities.

The following categories were included in the estimation of the quantity of CO from coal, gas, and oil combustion presented in Table 4–1: electric power utilities, coke plants, steel and rolling mills, cement mills, oil companies, other manufacturing and mining industries, military, residential, commercial, institutional, and light industrial. Emission factors are available for all categories but coke plants.

Coal and wood combustion account for the majority of CO emissions in the stationary combustion source category. Approximately 486 million tons of lignite and bituminous coal and 11.4 million tons of anthracite coal (excluding trains and ships) were consumed in the United States in 1966.[13] Electric power utilities and industries are the largest consumers of coal, but account for only about 25 percent of the emissions from this fuel. Total wood consumption by user category is not available. Total energy from wood combustion, however, was estimated to be 800 x 10^{12} Btu for 1966. Assuming 9,000 Btu per pound of wood, nearly 5.5 x 10^7 tons of wood were consumed resulting in an emission of approximately 1 million tons of CO as indicated in Table 4–1.

Approximately 568 million barrels of distillate fuel oil and 537 million barrels of residual fuel oil were consumed in stationary fuel combustion sources in 1966.[12] More than 60 percent of the total fuel oil is consumed for space-heating purposes in residential, commercial, institutional, and light industrial sources.

Total gas consumption, of which 99 percent consists of natural gas, exceeded 15,000 billion cubic feet in 1966.[15] Electrical power utilities consumed about 17 percent of the total with residential, commercial, institutional, military, and industrial sources accounting for the remainder.

3. Industrial Processes Producing Carbon Monoxide

Industrial processes emit varying quantities of CO into the atmosphere. The four largest sources of this pollutant are petroleum refineries, iron foundries, kraft pulp mills, and sintering plants. Other sources for which emission estimates were made are steel mills, lampblack plants, and formaldehyde manufacturers. Emission factors for these processes are based on analysis of sampling data; however, the lack of published data from other sources on production, types of equipment, and controls, as well as emission factors, make it impossible to include estimates of emissions for them. Some other sources of CO include ammonia and methanol reforming, synthesis gas manufacture, organic chemical manufacture (acids, esters, ketones, and aldehydes), reactive metals manufacture, and nonferrous secondary smelting.

The major source of CO in an iron foundry is the cupola. A questionnaire survey of the 1,450 foundries located in the United States indicates that 3.24 million tons of iron was charged to cupolas in 1966, with approximately 10 to 20 percent of this production subject to 90 percent afterburner control.

The major sources of CO in petroleum refining operations are the catalytic cracking units. The emissions of CO from roughly 75 percent of these units are nearly 100 percent controlled by waste heat boilers.

The major sources of CO in kraft paper mills are the lime kilns and the kraft recovery furnaces. The 23.6 million tons of pulp produced in 1966 from these sources emitted CO that was not subject to control.

The sintering of blast furnace feed is another major source of CO; 1968 production of both sinter and pellets is estimated to total 108 million tons.

The emissions from these major industrial sources were calculated as shown in Table 4–2.

4. Solid Waste Combustion

The total annual solid-waste production in the United States has been estimated to be about 357 million tons. About half of this solid waste is disposed of through incineration and open burning. This combustion results in the production of about 8 million tons of CO.

An estimate of the per-capita solid-waste generation rate was obtained from the results of a study by the National Center for Urban and Industrial Health on collected solid wastes[16] and from estimates by the National Air Pollution Control Administration on uncollected solid wastes. This estimate (10 lb/day per person), population figures, and information on the proportions of the various solid-waste disposal methods allowed estimation of the national CO emissions from this category.

5. Miscellaneous Combustion

The miscellaneous combustion category includes emission estimates from both uncontrolled and controlled forest fires, from agricultural waste burning, from structural fires, and from coal-refuse bank fires. These totals, however, do not include the burning of forest and crop residues.

The United States Forest Service estimates that over 4,570,000 acres of forest were destroyed by wild ("unprescribed") fires during 1966.[17] In addition, there were over 600,000 acres of controlled ("prescribed") burning in National parks. Prescribed burning by industry and private interest accounted for 2,920,000 acres. An average of 32 tons of wood per acre was burned in wild fires, and 22 tons per acre, in controlled fires. The total emission estimates presented in Tables 4–1 and 4–2 were calculated by applying an emission factor of 60 pounds per ton of burned material for agricultural open burning. In addition, 550 million tons of agricultural waste is generated each year.[16] It is estimated that half of this agricultural waste is burned in the open. Using an estimated emission factor of 60 pounds of CO per ton for open burning, the estimate for this source was calculated.

The National Fire Protection Association reports that more than a million buildings were attacked by fire in 1966 with a 20 to 30 percent extent of destruction. The CO emissions from structural fires were estimated using these assumptions and an average emission factor for wood burning of 45 pounds per ton.

The Bureau of Mines estimates that 19 billion cubic feet of burning coal refuse piles existed in the United States in 1966, that the density of these coal piles averages 100 pounds per cubic foot, and that, on the average, one of these coal banks will burn for 20 years.[18] With these assumptions, the emissions from this source were estimated using an emission factor for coal combustion of 50 pounds of CO per ton of coal burned.

D. PROJECTIONS OF CARBON MONOXIDE EMISSION LEVELS

Two factors must be considered in projecting future CO emission levels. The first is the potential increases caused by population growth–more motor vehicles and aircraft, expansion of industry, and the increased use of fuel combustion for power and heat to be expected in the coming decades. The second, and opposing, factor is the application of more effective control technology. For the major national CO emitter, motor vehicles, no further increase in the magnitude of CO emissions would be expected before 2000 because of present and anticipated (1970) CO control measures required by existing Federal Statutes. Future trends are depicted in Figure 4–2.

No projections have been made for CO emissions from stationary sources because of lack of published data. The national magnitude of CO emissions from these sources is expected to increase, although it is recognized that changes in fuels, industrial processes, and methods of solid waste disposal may result in decreases in CO emissions from specific sources.

E. SUMMARY

Annual carbon monoxide emissions from major sources in the United States are estimated to be 92 x 10^9 kilograms (102 million tons) for the year 1968. The largest single source was the gasoline-powered motor vehicle, which accounted for 54 x 10^9 kilograms (59 million tons), or over 58 percent of the total. Internal combustion engine sources used in aircraft, non-highway use, trains, ships, and diesel-powered motor vehicles accounted for another 5 percent of the total. Other major sources included fuel combustion in stationary sources, industrial processes, solid waste combustion, and forest fires.

Carbon monoxide emission totals were found to differ among different regions of the United States, estimates ranged up to about 5 x 10^9 kilograms (5 million tons) per year in New York and Los Angeles. In all but two of 26 cities surveyed, the CO emissions were the largest component of the total tonnage of pollutants emitted to the atmosphere. The major source of CO emissions in all of the regions studied was the motor vehicle.

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CHAPTER 5.

MEASUREMENT OF CARBON MONOXIDE CONCENTRATIONS IN AMBIENT AIR

A. INTRODUCTION

Because of the need to measure the wide range of CO concentrations found in community air (from less than 1 to about 150 mg/m^3), numerous measurement techniques have been developed. Standardization of CO in air samples for measurement, and subsequent measurement by available aerometric techniques are discussed in this chapter. Gas samples may be standardized by volumetric, gravimetric, and chemical techniques. The methods available for continuous measurement of CO include: (1) nondispersive infrared (NDIR) analysis, (2) electrochemical analysis, (3) mercury vapor analysis, (4) gas chromatography, and (5) catalytic and electrolytic analysis. The methods available for spot or integrated measurements include: (1) nondispersive infrared analysis, (2) infrared spectrophotometric analysis, (3) gas chromatographic analysis, and (4) colorimetric analysis.

Several tentative methods for the determination of CO in ambient air have been prepared for collaborative testing and evaluation as possible standards by the Intersociety Committee on Manual of Methods of Air Sampling and Analysis. Hopefully, one or more of these methods will qualify as a standard method against which all instruments and methods may be calibrated.[1]

B. PREPARATION OF CARBON MONOXIDE GAS STANDARDS

1. Volumetric Gas Dilution Techniques

Accurately prepared CO gas standards must be available for the calibration of methods and measuring instruments before CO can be quantified. Volumetric gas dilution is the technique used most frequently for the preparation of standards. If a large quantity of standard gas is needed, the dilution may be made in pressurized tanks.[2,3] Care should be exercised to assure accuracy of the standard because CO in pressurized tanks may be unstable at concentrations of less than 1 milligram per cubic meter (1 ppm).

A known volume of CO is placed in an evacuated tank of known volume, and the tank is subsequently filled to a known pressure with CO-free nitrogen or helium. The concentration of CO in the tank may then be calculated. Standard samples in 5- to 100-liter volumes also may be prepared in plastic bags.[4] The diluent gas is metered into an evacuated plastic bag with a suitable device; and as it flows into the bag, a measured volume of pure CO is injected by syringe into the line connecting the metering device to the bag. The concentration is calculated from the total volumes of diluent gas and CO in the bag.

It is important in these operations to verify that the diluting gas is free of CO. Some investigators suggest that pure helium, which is reliably free of CO, is preferable to nitrogen as a diluent. A less expensive method is to use helium periodically as a true "zero" gas to estimate the CO content in the nitrogen diluent. A correction factor is then used to account for the CO content in the nitrogen.

2. Gravimetric Methods for Standardizing Carbon Monoxide Gas Mixtures

Gravimetric methods are not used routinely in air pollution studies to measure CO because relatively large samples are needed to quantify CO concentrations. These methods are useful, however, for checking CO standards. McCullough et al.[5] made use of the reaction:

$$\text{CO(gas)} + \text{HgO (solid, red)} \xrightarrow{(175^\circ\text{-}200^\circ\text{C})} \text{Hg(gas)} + \text{CO}_2\text{ (gas)}.$$

During the passage of the gas sample, the red mercuric oxide is reduced and loses weight. This weight loss and the measured volume of the sample are used to calculate the concentration of CO present in the standard gas mixture.

Salsbury et al.[6] used a method in which the gas containing CO is drawn over Hopcalite at 195°C and the carbon dioxide formed is absorbed in tubes containing Ascarite. Gas volumes are determined using a flowmeter and a stopwatch. From the weight of the CO_2 absorbed in the tubes, the CO concentration is calculated. This method is accurate to about 2 percent for CO concentrations of from 25 to 1000 milligrams per cubic meter (22 to 870 ppm).

Lysyj et al.[7] oxidized CO to CO_2 with decomposed silver permanganate ($AgMnO_4$) as a catalyst and weighed the CO_2 absorbed in an Ascarite tube.

3. Chemical Assay of Carbon Monoxide Gas Standards

The reduction of iodine pentoxide may be used to measure CO in standard gas mixtures. Adams and Simmons[8] have given a detailed discussion of the method. The analysis is based on the reaction:

$$5\,CO + I_2O_5 \rightarrow 5\,CO_2 + I_2.$$

When the gas mixture containing CO is passed over heated I_2O_5, iodine is liberated. It is then collected and titrated with standard sodium thiosulfate.

C. MEASURING CARBON MONOXIDE IN ATMOSPHERE

1. Continuous Measurement of Carbon Monoxide

a. Definitions of Terms Describing Instrument Performance

Definitions of some terms commonly used to describe instrument performance are given below; in this document these terms will be used as defined throughout this chapter.

Sensitivity. The smallest change in pollutant concentration that can be detected.

Minimum detectable concentration. The sensitivity as the pollutant concentration approaches zero.

Response time. The amount of time taken by an instrument from the start of a change in input before the instrument output reaches a specified percentage of the ultimate change. (The specified percentage is usually 90 or 95). The response time is a measure of the minimum averaging time necessary to achieve valid output data.

Lag time. The time between the start of an input signal and the observed start of the output response corresponding to that signal. The lag time is a measure of the delay between input sample and output data, and is always less than or equal to the response time.

Accuracy. The degree of agreement of the true value with the indicated value or values.

True value. The number that is completely consistent with the (known) value and definition of the primary standard used.

b. Nondispersive Infrared Analyzers

Nondispersive infrared (NDIR) analyzers are the most commonly used continuous, automated devices for determining atmospheric CO and are generally accepted as being the most reliable reference method for the calibration of other instruments. An NDIR analyzer operates on the principle that CO has a sufficiently characteristic infrared absorption spectrum that the absorption of infrared radiation by the CO molecule can be used as a measure of CO concentration in the presence of other gases. Although the size, shape, sensitivity, and range of these instruments vary with manufacturer, basic components and configurations are similar. Most commercially available instruments include a hot filament source of infrared radiation, a rotating sector (chopper), a sample cell, a reference cell, and a detector. The detector senses pressure changes on either side of a diaphragm separating portions of gases being irradiated through the sample cell or the reference cell of the instrument. These pressure changes are converted to electrical signals corresponding to the difference between radiation received from the sample and reference cells. The signal is amplified and rectified, and then read on a meter or recorder calibrated to yield CO concentration.

Most commercially available instruments function on the double-beam principle, operate at atmospheric pressure, and are able to detect minimum CO concentrations of about 0.6 to 1.2 milligrams per cubic meter (0.5 to 1.0 ppm). The sensitivity of NDIR instruments and the minimum concentrations they can detect are proportional to the length of the cells, electronic amplification, and operating pressures. Measuring ranges usually extend from 1 to 58 mg/m^3 (1 to 50 ppm) CO or from 1 to 115 mg/m^3 (1 to 100 ppm) CO. Newer NDIR instruments, however, may be operated at from 1 to 29 mg/m^3 (1 to 25 ppm) CO at atmospheric pressure and with cell path lengths of less than 0.5 meter.

NDIR analyzer response times are determined by the physical dimensions of the system, the flow rate of the sample, and the response time of the meter or recorder. Response times may range from less than 1 to 5 minutes.

Carbon dioxide and water vapor interfere in the determination of CO by NDIR techniques. Filter cells are used to minimize these interferences. They may be placed in front of the sample cell or in front of both sample and reference cells. Filter cells, filled with carbon dioxide (CO_2) and water vapor, absorb radiation at interfering wavelengths so that normal atmospheric concentrations of CO_2 and water vapor in the sample have minimal effect on the radiation reaching the detector.[9]

Optical filters are also used successfully to limit the infrared wavelength and bandwidth to a range in which CO_2 and water vapor are transparent and thus invisible to the instrument.

Other techniques may be used to minimize or prevent CO_2 interference. Ascarite-filled tubes remove CO_2 from the entering gas stream; other systems add nominal quantities of CO_2 (300 to 400 ppm) to the zero and span gases used to calibrate the NDIR instrument.

Filter cells reduce water vapor interference; however, they do not adequately cope with the high absolute humidities frequently encountered in atmospheric monitoring. Figure 5-1 shows the effect of water vapor on a typical NDIR analyzer uncompensated for water vapor interference.[10] Air streams may be dried by using dehydrating agents such as silica gel, anhydrous calcium sulfate, magnesium perchlorate, or combinations of these media.[11,12] Jacobs et al.[13] found, however, anhydrous calcium sulfate to be unsatisfactory for the removal of water vapor from the gas stream. Satisfactory results were obtained by saturating the incoming air with water at a constant temperature, thus eliminating water as a variable. Some commercially available instrument systems use this technique to eliminate water vapor interference. Others reduce water vapor interference by passing the air sample through a refrigerator in front of the analytical system to condense moisture from the air. This system, however, cannot regulate the absolute humidity in the air stream undergoing analysis when the dew

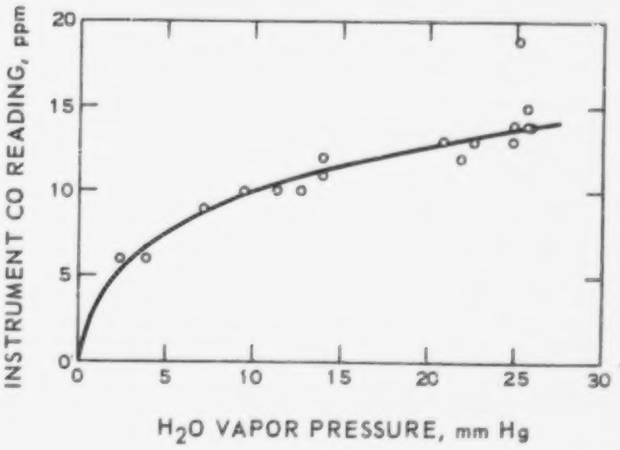

Figure 5-1. Typical nondispersive infrared analyzer response to water vapor.[10]

point of the sample air is lower than the refrigerator temperature (as is the case in cold weather or with pressurized calibration gases). It should be realized that most methods of reducing CO_2 and water vapor interferences also tend to reduce instrument sensitivity or increase instrument response time, or both.

NDIR systems have several advantages. They are not sensitive to flow rate, they require no wet chemicals, they are reasonably independent of ambient air temperature changes, they are sensitive over wide concentration ranges, and they have short response times. Further, NDIR systems may be operated by nontechnical personnel. Such systems also have some disadvantages, such as zero drift, span drift, nonlinearity, and high cost. Some newer instruments have minimum drift because good quality thermostats and solid-state electronics are used in their manufacture. Such instruments also have automatic zeroing, spanning, and recalibrating capability; they may also be obtained with essentially linear outputs. Features such as these should be considered when multiple-station networks are established.

c. *Electrochemical Analyzers*

(1). Galvanic analyzer. Galvanic cells employed in the manner described by Hersch[14,15] can be used to measure atmospheric CO continuously. When an air stream containing CO is passed into a chamber packed with I_2O_5 and heated to 150°C, the following reaction takes place:

$$5CO + I_2O_5 \xrightarrow{(150°C)} 5CO_2 + I_2.$$

The liberated iodine is absorbed by an electrolyte and transferred to the cathode of a galvanic cell. At the cathode, the iodine is reduced, and the resulting current is measured by a galvanometer. Instruments using this detection system have been used successfully to measure CO levels in traffic along freeways.[16]

Mercaptans, hydrogen sulfide, hydrogen, olefins, acetylenes, and water vapor interfere. Water may be removed by sampling through a drying column; hydrogen, hydrogen sulfide, acetylene, and olefin interferences can be minimized by sampling through an absorption tube containing mercuric sulfate ($HgSO_4$) on silica gel.

(2). Coulometric analyzer. A coulometric method employing a modified Hersch-type cell has been used to measure CO in ambient air on a continuous basis.[12] The iodine pentoxide (I_2O_5) reaction with CO liberates iodine, which is then passed into a Ditte cell, and the current generated is measured by an electrometer-recorder combination. Interferences are the same as those discussed above for the galvanic analyzer.[17,18]

This technique may be used for a minimum detectable concentration of 1 milligram per cubic meter (1 ppm) with good reproducibility and accuracy if flow rates and temperatures are well controlled. This method requires careful column preparation and use of filters to remove interferences. Its relatively slow response time may be an added disadvantage in some work.

d. *Mercury Vapor Analyzer*

A continuous CO analyzer using the reaction of CO with hot mercuric oxide and photometric determination of the mercury vapor produced has been developed and used.[11] The reaction involved is:

$$CO + HgO\ (s) \xrightarrow{(210°C)} CO_2 + Hg(g).$$

Oxygenated hydrocarbons and olefins react quantitatively and, therefore, present a major interference; however, these are normally present in the ambient atmosphere in low concentrations relative to CO. Free hydrogen also interferes with the technique, but this interference is not serious because very little free hydrogen is present in the air. The effect of ozone is not reported, but ozone, too, is normally present in the atmosphere in very low concentrations relative to CO.

The mercury vapor instrument has a response time similar to that of the NDIR analyzer; but because of interferences and some electronic instability, it does not appear to be suitable for routine urban atmospheric monitoring. The instrument is, however, a useful, portable, continuous analyzer with a capability for analyzing concentrations of from 0.029 to 11.5 milligrams of CO per cubic meter (0.025 to 10.0 ppm). Changes of 0.002 mg/m^3 (0.002 ppm) are detectable. For this reason it has found application in determining geophysical "background" CO levels throughout the world.

e. Gas Chromatographic Analyzer

A prototype automated gas chromatographic system has been developed to measure both CO and methane.[19] A gas sampling valve, a back flush valve, a precolumn, a molecular sieve column, a catalytic reactor, and a flame ionization detector comprise the system. The precolumn prevents CO_2, water, and hydrocarbons other than methane from reaching the molecular sieve. The catalytic reactor quantitatively converts CO to methane, which is then measured by the flame ionization detector. The system is designed for semicontinuous operation with the capability of performing one analysis about every 5 minutes. It has a linear output for both CO and methane, and has a wide operating range suggesting its use in both heavily polluted areas and relatively clean locations. Simultaneous CO and methane concentrations of from 0.1 to 1,000 ppm may be measured with this instrument. Its semicontinuous characteristics suggest its use in special surveys and field studies rather than for routine air monitoring. The fact that the instrument must be operated by technically trained personnel may be considered a possible disadvantage.

f. Catalytic Analysis

Carbon monoxide may be oxidized catalytically to CO_2 using Hopcalite; the resulting temperature rise is recorded continuously and is used to indicate CO concentrations.[20,21] These systems are widely used in enclosed spaces; their applicability for ambient air monitoring is limited because they function best at high ambient concentrations.

2. **Intermittent Analysis**

a. Collection of Spot or Integrated Samples

Intermittent samples may be collected in the field and later analyzed in the laboratory. A detailed outline of this technique has been given by Mueller.[22] Sample containers may be rigid (glass cylinders or stainless steel tanks) or they may be non-rigid (plastic bags). Because of location or cost, intermittent sampling at times may be the only practical method for air monitoring. Samples can be taken over a few minutes or accumulated intermittently to obtain, after analysis, either "spot" or "integrated" results. Techniques for analyzing intermittent samples are described below.

b. Nondispersive Infrared Analysis

Field NDIR continuous monitoring analyzers discussed previously can be used for laboratory analysis of intermittent samples. NDIR instruments are designed by some manufacturers primarily for use in the laboratory and must be modified for continuous ambient air monitoring in the field.

c. Infrared Spectrophotometric Analysis

Carbon monoxide may be measured by its infrared absorption at 4.6 microns. Other gases may absorb at 4.6 microns, but they can be differentiated from CO by examining the complete spectrum from 2 to 15 microns. The sensitivity and range of the technique depends on the sophistication of the instrument used. A minimum detectable concentration of 2.9 milligrams per cubic meter (2.5 ppm) CO has been obtained by instruments using scale expansion and a 1-meter path-length cell.[23] It can be expected that a similar infrared spectrophotometer equipped with a 10-meter cell and ordinate scale expansion would have a 0.3-milligram-per-cubic-meter (0.3 ppm) CO detection capability. Water vapor and CO_2 must be removed from the sample before the infrared scan can be made; in most applications magnesium perchlorate and Ascarite are used to remove interfering substances. The technique is specific and accurate, but requires expensive, nonportable equipment.

d. *Gas Chromatographic Analysis*

After reduction of CO over a reduced nickel catalyst, a gas chromatograph equipped with a flame ionization detector, discussed earlier, becomes a satisfactory tool for determining low levels of CO.[10,19,24-26] One mole of CO produces 1 mole of methane. Since methane may be detected at concentrations of about 0.01 ppm, it is possible to detect such a concentration of CO.[27] The technique does not suffer from interferences because the measurement is made on a methane peak derived from a separated CO peak. Operating temperatures and other parameters must be controlled, however, before reliable results can be obtained.

e. *Colorimetric Analysis*

(1). Colored silver sol method. Carbon monoxide reacts in an alkaline solution with the silver salt of p-sulfamoylbenzoate to form a colored silver sol. Concentrations of from 12 to 23,000 milligrams per cubic meter (10 to 20,000 ppm) CO may be measured by this method.[28-32] The procedure has been modified to determine CO concentrations in incinerator effluents.[17] Samples are collected in an evacuated flask and reacted. The absorbance of the resulting colloidal solution is measured spectrophotometrically. Acetylene and formaldehyde interfere, but can be removed by passing the sample through mercuric sulfate on silica gel. Carbon monoxide concentrations of from 6 to 20,700 milligrams per cubic meter (5 to 18,000 ppm) may be measured with an accuracy of 90 to 100 percent of the true value.

(2). National Bureau of Standards colorimetric indicating gel. A National Bureau of Standards (NBS) colorimetric indicating gel (incorporating palladium and molybdenum salts) has been devised to measure CO in the laboratory and in the field.[33,34] The laboratory method involves colorimetric comparison with freshly prepared indicating gels exposed to known concentrations to CO. The method has an accuracy range of from 5 to 10 percent of the amount of CO involved, and the minimum detectable concentration is 0.1 milligram per cubic meter (0.1 ppm). This technique requires relatively simple and inexpensive equipment; but oxidizing and reducing gases interfere, and the preparation of the indicator tube is a tedious and time-consuming task.

(3). Length-of-stain indicator tube. An indicator tube method using potassium pallado-sulfite is a commonly used manual method.[35] Carbon monoxide reacts with the contents of the tube and produces a discoloration. The length of discoloration is an exponential function of the CO concentration. This method and other indicator tube manual methods are estimated to be accurate to within ± 25 percent of the amount present, particularly at CO concentrations of about 115 milligrams per cubic meter (100 ppm). Such indicator tube manual methods have been used frequently in air pollution studies. Ramsey[36] used the technique to measure CO at traffic intersections, and Brice and Roesler[37] used color-shade detector tubes to estimate CO concentrations with an accuracy of ±15 percent.

Colorimetric techniques and length-of-stain discoloration methods are recommended for use only when the other physiochemical monitoring systems are not available. They may be used in the field for gross mapping where accuracy is not required and might be of great value during emergencies.

D. SUMMARY

Because CO levels exist over such a wide concentration range, the use of a variety of chemical and physical procedures may be required to evaluate atmospheric concentrations fully and accurately. The accuracy of any aerometric method used can be no better than the standards used to calibrate the instrument used. When pure CO and CO-free nitrogen are available, volumetric gas dilution techniques are satisfactory ways to prepare standard gases. Gas mixtures of doubtful or unknown concentrations of CO may be assayed by the gravimetric and chemical (iodine pentoxide) standardization methods, which are time-consuming, but accurate.

The continuous measurement of atmospheric CO can be accomplished by using a variety of techniques. The most commonly used device is the nondispersive infrared (NDIR) analyzer, which is reasonably sensitive, but subject to a number of interferences. These interferences may be removed or minimized by proper treatment of the air stream.

New NDIR analyzers have the capability of measuring CO in the range of from 1 to 29 milligrams per cubic meter (1 to 25 ppm), and they may be equipped with automatic zeroing, spanning, and calibrating equipment; also, they are linear in output. All NDIR systems have the advantages of being insensitive to flow rates, requiring no wet chemicals, and being reasonably independent of ambient air temperature changes if the instrument is properly thermostatted. The NDIR analyzer is generally accepted as being the most reliable reference method for the calibration of other instruments.

Continuous CO monitoring instruments based on galvanic and coulometric principles have not been used extensively in field operations. They are flow- and temperature-dependent, and require the use of filters to remove multiple interferences.

The mercury vapor analyzer, which depends on the liberation of mercury vapor when CO is passed over hot mercuric oxide, has been used as a portable, continuous monitoring analyzer with a special capability for measuring low CO concentrations (0.29 milligram per cubic meter, or 0.25 ppm). The instrument does not appear to be suitable for routine CO monitoring of urban atmospheres.

The automated gas chromatographic system is semicontinuous in operation, but has the advantage of measuring both CO and methane. Concentrations of from 0.1 to 1,150 milligrams per cubic meter (0.1 to 1000 ppm) may be determined, and instrument output for both gases is linear over the range mentioned. Instruments of this kind may be available soon, and it appears this technique will be useful for measuring CO in heavily polluted areas as well as at remote, relatively clean locations.

CO monitoring systems based on catalytic conversion principles are used widely in enclosed spaces, but their applicability for ambient air monitoring is limited.

Colorimetric (colored silver sols) methods are not recommended for monitoring ambient air. The approach may be useful, however, for measuring CO in stack effluents. Colorimetric techniques and length-of-stain discoloration methods are recommended for use only when the above-mentioned physiochemical systems are not available. They may be used in the field for gross mapping where accuracy is not required and might be of great value during emergencies.

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CHAPTER 6.

ATMOSPHERIC CARBON MONOXIDE CONCENTRATIONS

A. INTRODUCTION

The concentration of CO in urban communities varies widely with time and location. Continuous monitoring for CO has been conducted at stations operated by the National Air Pollution Control Administration's Continuous Air Monitoring Program (CAMP), the State of California, and Los Angeles County. These efforts and special studies have made it possible to discern some patterns in CO concentration variations.

Statistical analysis techniques have led to the development of methods for analyzing CO concentration data. From CO monitoring information for a given location, the frequency of occurrence of a specific CO concentration can be estimated. Further, theoretical diffusion models may clarify CO patterns and help in predictions.

B. TEMPORAL VARIATIONS IN CARBON MONOXIDE CONCENTRATIONS

1. Diurnal Patterns

Community CO levels follow a regular diurnal pattern of variation dependent primarily on human activity.[1-5] Ambient CO concentrations generally correlate well with traffic volume; the highest correlations and levels are associated with measurements taken where vehicular traffic is heaviest.

While the exact shape and magnitude of the diurnal CO curve for a community is dependent to a large extent on meteorologic factors, two peaks corresponding with the morning and evening traffic "rush" hours are usually detectable. See Figures 6–1 and 6–2. Carbon monoxide levels in most cities reach their initial daily maximum between 7:00 and 9:00 a.m., coincident with heavy morning automobile traffic. Another peak is reached in the late afternoon and early evening hours.[1,2,4,5] Although a late afternoon rise is evident at all monitoring sites depicted in Figures 6–1 and 6–2, a distinct evening rush-hour peak is not evident from the Los Angeles data. This situation probably resulted from the greater wind speed in Los Angeles in the afternoon, usually about twice the wind speed in the morning.[6]

An exception to these general observations may be found in "downtown" New York City, where there is a rapid rise in the morning corresponding to the morning rush hour traffic, then a constant plateau that lasts until afternoon when a slower rise begins and builds to a peak in late afternoon. See Figure 6–3. The shape of the traffic curve seen in this figure is indicative of saturation levels of traffic.[7]

The diurnal pattern within a community, being directly related to traffic volume, shows little variation with day of the week except for weekends and holidays. The weekday concentrations are higher than those recorded on Saturdays, which are higher than those recorded on Sundays and holidays.[2-4,6] Colucci and Begeman, sampling at a variety of sites in Detroit, New York, and Los Angeles, found that, in general, the average CO concentration on Saturdays and Sundays was about 20 percent less than that on weekdays.[6] Changes in traffic volume resulting from changes in human activities were found to be responsible for these variations. For example, only at the freeway sites sampled in New York and Los Angeles did the weekend average equal or exceed the weekday average. The diurnal variations of CO concentrations

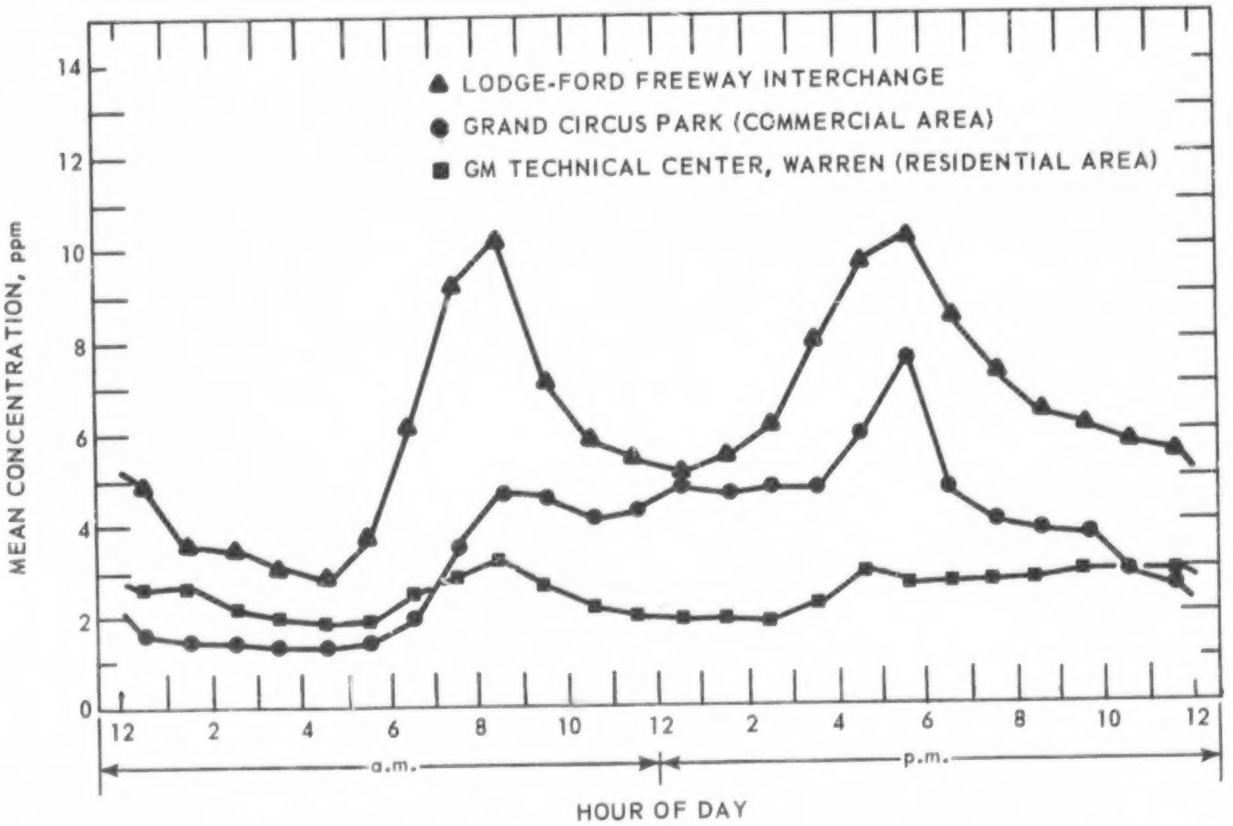

Figure 6-1. Diurnal variation of carbon monoxide levels on weekdays in Detroit.[6]

on weekdays, Saturdays, and Sundays are shown for the Chicago CAMP station in Figure 6–4.

The variation of atmospheric levels of CO with traffic density was studied by Brief, Jones, and Yoder at six locations in a Northeastern metropolitan city of the United States.[3] Based on 30 data points, these investigators found that CO concentrations showed a linear correlation with traffic density. The CO levels were correspondingly lower on Sundays where the average traffic flow was reduced by one-third to one-half the overall weekday station average. Figure 6–5 depicts the regression line found by these investigators along with the corresponding 95 percent confidence limits for the regression of atmospheric CO concentration on traffic density. The extent to which the correlations and confidence intervals can be generalized in other cities varies with such factors as meteorology, type of traffic flow, and the influence of other sources.[3] Under conditions (not experienced during these tests) of high wind and vertical turbulence, which promote maximum dilution, the slope of the correlation curve could be lessened so that even under conditions of high traffic density, the levels of CO might be below the lower confidence limits. On the other hand, in an area with predominantly stagnant weather conditions, the slope of the correlation curve might be greater than that shown in Figure 6–5.

In their studies in Detroit, New York, and Los Angeles, Colucci and Begeman found correlation coefficients between CO concentrations and traffic counts ranged from 0.75 to 0.95.[6] Similar analyses have been conducted by others.[7-9]

The intimate relationship between urban CO concentrations and traffic conditions represents a means of practical CO emission control beyond the specific engineering controls on individual vehicles. As was indicated in Chapter 4, an increase in average automobile speeds in urban driving reduces CO emissions. It should be possible to capitalize on this fact in city planning by designing to

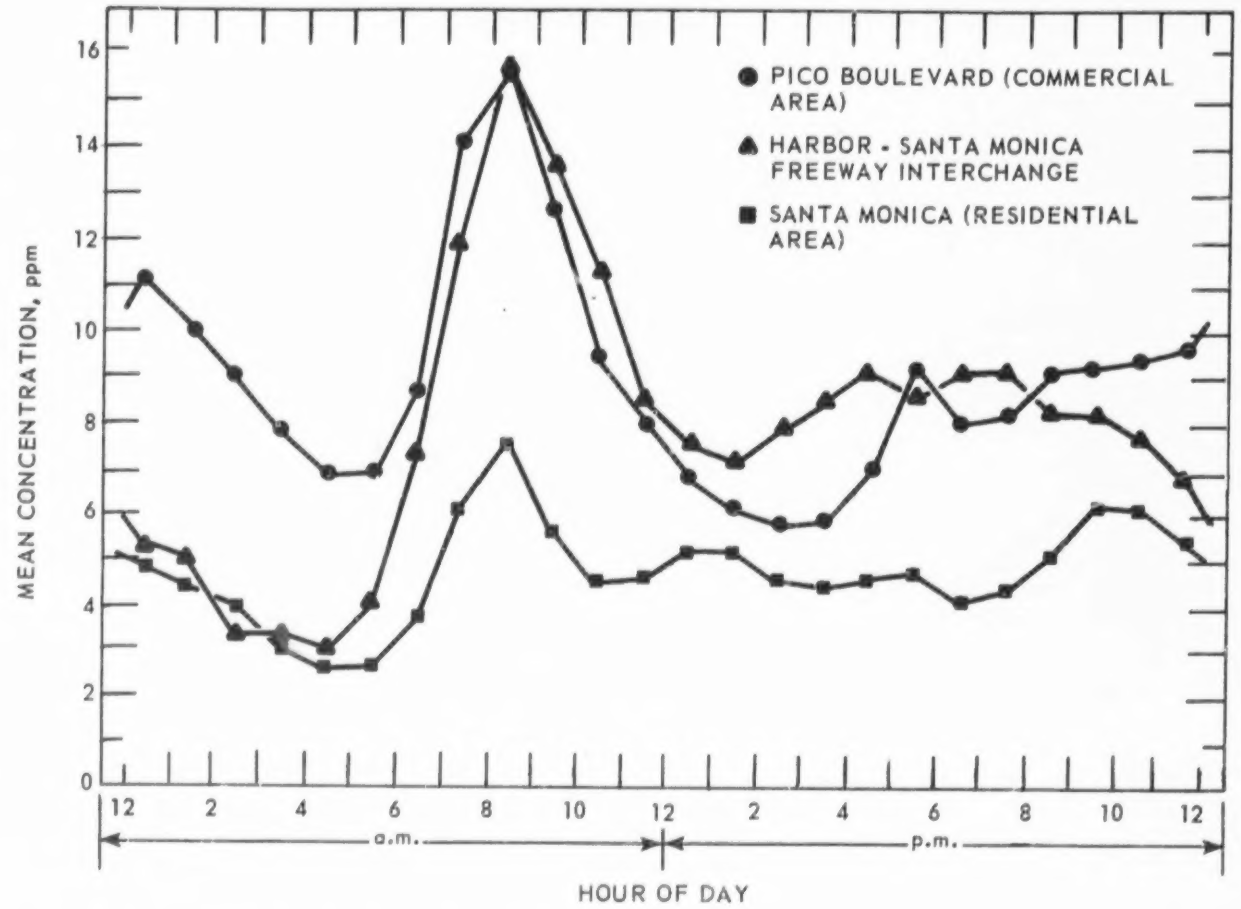

Figure 6-2. Diurnal variation of carbon monoxide levels on week days in Los Angeles.[6]

increase speed and continuity of traffic through central urban areas.

2. Seasonal Patterns

Community atmospheric CO levels reveal seasonal patterns, which result primarily from changes in meteorologic parameters. CAMP data for the years 1964 through 1967 indicate that CO concentrations are generally highest in the fall, followed by the summer, spring, and winter, respectively.[10] The tendency toward increased atmospheric stability and low wind speeds in the two former seasons contribute a substantial part to the occurrence of high CO concentrations.

3. Annual Variations

The data available for studying differences by year and trends of CO concentrations are shown in Tables 6–1 through 6–3. Calculations from continuous measurements at 46 sampling sites (located mainly in California) indicate that no essential change in annual average concentrations occured from year to year. To be sure, there were average annual changes of 1 milligram per cubic meter (1 ppm) up or down, but there does not appear to be any consistent upward or downward trend in annual average CO concentrations.

It has been noted, however, that for some California stations associated with marked population increases, significant increases in CO concentrations were observed during the first few years of sampling.

C. EFFECT OF METEOROLOGICAL FACTORS

The rate of emission and dispersion determine the concentration of a pollutant at a given location. Both macro- and micrometeorological factors play a role in the rate of dispersion of CO emissions. For dispersion over short distances, microscale factors are most important,[1,8] but over extended distances, macroscale factors dominate. The

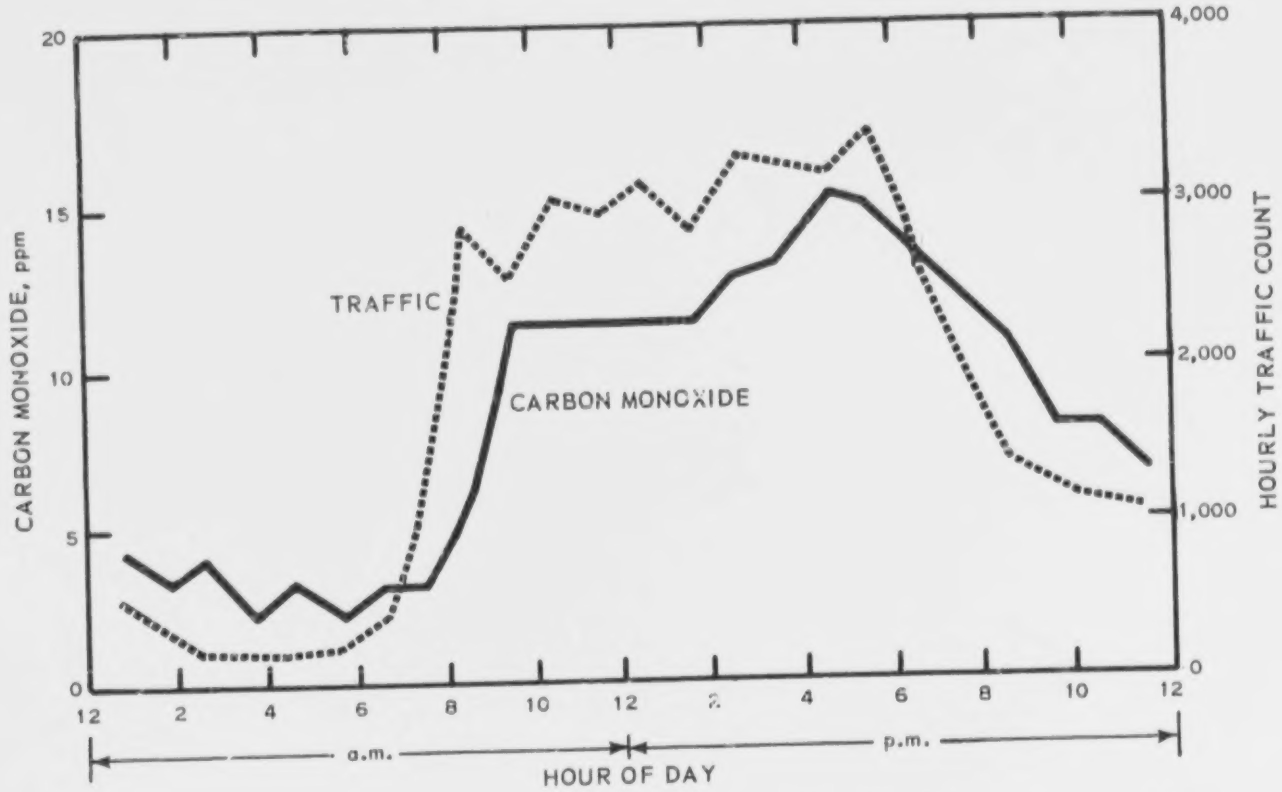

Figure 6-3. Hourly average carbon monoxide concentration and traffic count in mid-town Manhattan.[7]

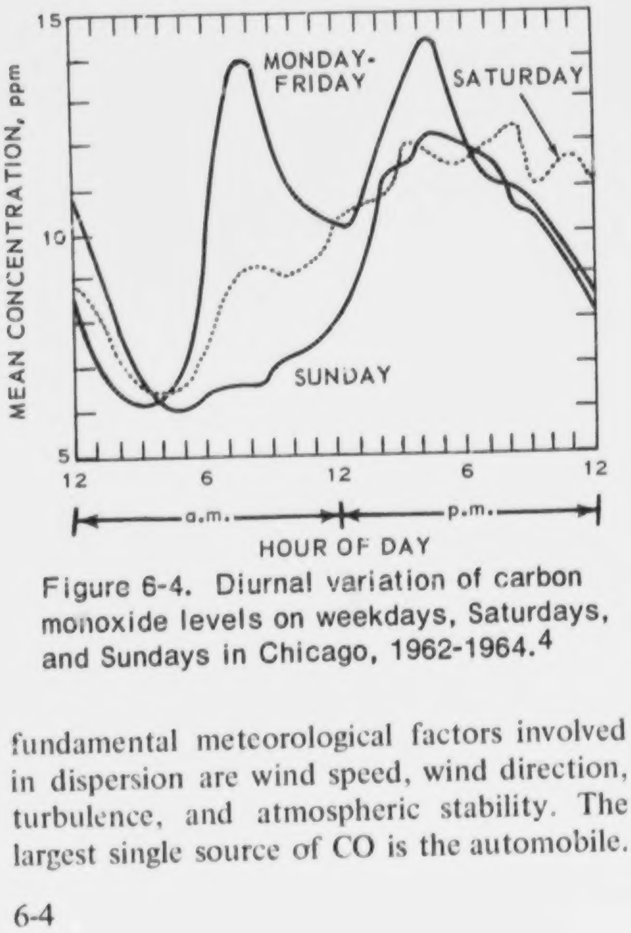

Figure 6-4. Diurnal variation of carbon monoxide levels on weekdays, Saturdays, and Sundays in Chicago, 1962-1964.[4]

fundamental meteorological factors involved in dispersion are wind speed, wind direction, turbulence, and atmospheric stability. The largest single source of CO is the automobile.

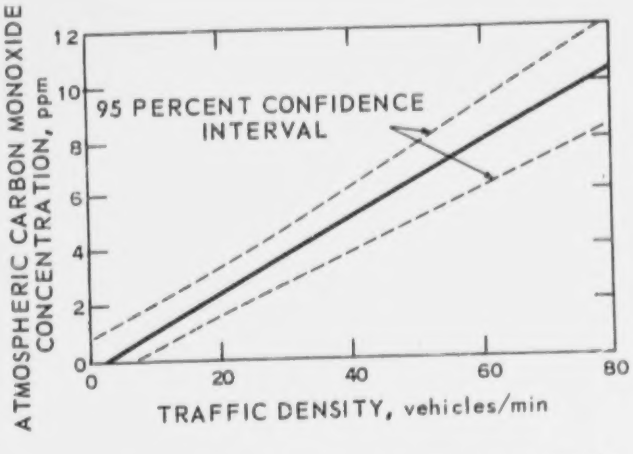

Figure 6-5. Correlation of carbon monoxide concentration and traffic density.[3]

Logically, the greatest emissions are expected to be found on city streets when traffic volume is high. On city streets where people are close to sources, the micrometeorological factors become critical in determining exposures.

Because automobiles usually are moving and create their own rather small, but intense, field of mechanical turbulence, the diffusion resulting therefrom is important in the determination of neaby CO concentrations. This is particularly true when the wind speed is low (mean wind speed of $\leq$ 1.3 m/sec or 3 mi/hr).[8,11] When there are high wind speeds, the air flowing over and around buildings adds turbulence and mixing to that generated by vehicles. Higher wind speeds, therefore, increase turbulence and dilution, and thereby generally lower pollutant concentrations.

During prolonged periods of air stagnation, which do occur in most urban communities periodically, poor or inadequate diffusion, contributes to the buildup of atmospheric levels of CO and other air pollutants. In the Fall of 1964, during unusually prolonged and severe inversions, CO concentrations in Los Angeles and in Sacramento, California, exceeded 35 mg/m^3 (30 ppm) for 8 hours.[12] In the results of sampling done in London from October 1956 to October 1957, Lawther et al. reported a peak CO reading of 270 mg/m^3 (235 ppm) measured on a traffic island and a level of 415 mg/m^3 (360 ppm) CO measured on a calm day at another street-level location.[13] In 1967, of 15,216 samples from 317 locations in Paris, 235 exceeded 115 mg/m^3 (100 ppm) CO. Of these, 11 were equal to or greater than 345 mg/m^3 (300 ppm). 21 were between 230 and 345 mg/m^3 (200 and 300 ppm), and 203 were between 115 and 230 mg/m^3 (100 and 200 ppm).[14]

Because smog is indicative of air stagnation conditions, a comparison of CO levels on smoggy and nonsmoggy days is of interest. Based on sampling in a moving vehicle (with the intake level about 5 feet above the street) Castrop[15] et al. reported that the mean CO concentrations at street level were 11.1 mg/m^3 (9.7 ppm) CO for nonsmoggy days and 45.3 mg/m^3 (39.4 ppm) for smoggy days (defined visually). The highest concentration detected, 135 mg/m^3 (160 ppm), occurred during a smog period.

A similar analysis of stationary CO measurements in a Log Angeles commercial area showed that the average CO concentration on 21 smoggy days (defined by a 1-hour oxidant concentration greater than or equal to 0.15 ppm) was 13.2 mg/m^3 (11.5 ppm) versus 6.9 mg/m^3 (6 ppm) recorded on 16 smogless days.[6]

The concentration of CO in the vicinity of a city street is the product of emissions not only on that street but also from streets upwind. Accordingly, the "background" concentration from more distant sources depends for the most part on the number of streets upwind acting as CO sources and the macrometeorological factors mentioned previously.

D. OBSERVED URBAN CARBON MONOXIDE CONCENTRATIONS

1. Sources of Data

Continuous, automatically recorded CO data are available for selected cities in the United States from metropolitan monitoring stations of the Continuous Air Monitoring Program (CAMP). See Tables 6–1 and 6–4. Similar data are also available from the State of California for 23 communities (Table 6–2) and 28 local sites in Los Angeles County (Table 6–3). Because all of these stations use similar recording equipment and techniques, some basis for comparison of CO data exists.

2. Techniques of Data Analysis

a. Introduction

The collection of air quality data is of little value unless these data are properly analyzed. For this reason, the method of analysis to be applied should be clearly defined before sampling is begun. In fact, the data acquisition process itself should be determined by techniques of analysis available. Careful examination may show that a proposed sampling scheme may be unsatisfactory for acquiring data for the desired purpose or may even provide entirely irrelevant information.

The purpose of the following discussion of data analysis techniques is threefold: (1) to indicate those data parameters frequently

Table 6–1. CARBON MONOXIDE CONCENTRATION AT CAMP SITES, BY AVERAGING TIME AND FREQUENCY, 1962 THROUGH 1967
(ppm)

City and averaging time	1962–1967					Maximum for year						% data avail	% of time concentration is exceeded:								
	Annl max	Geo mean	SGD	Maxima																	
				Max	Min	62	63	64	65	66	67		0.001	0.01	0.1	1	10	30	50	70	90
Chicago																					
5 min	81	13.0	1.51	78	43	43	50	64	61	78	63	53	69	58	45	34	22	16	11	8	4
1 hr	54	13.2	1.44	59	28	28	36	46	44	59	56	54		54	41	31	22	16	12	8	4
8 hr	39	13.4	1.38	44	20	20	22	35	37	44	33	55			35	27	21	16	12	8	5
1 day	33	13.5	1.34	33	17	17	19	27	32	33	23	55				25	20	15	12	8	5
1 mo	19	13.9	1.21	21	7	7	10	17	21	18	11	60					18	15	11	9	7
1 yr	14	14.1	1.00	17	12			12	17	13		50							12		
Cincinnati																					
5 min	43	4.6	1.66	50	26			26	50	32	47	72	45	31	21	15	9	6	4	3	2
1 hr	27	4.8	1.57	34	20			22	34	20	27	73		27	19	15	9	6	5	3	2
8 hr	18	4.9	1.48	21	12			19	21	12	17	74			18	14	8	6	5	4	2
1 day	14	4.9	1.44	17	9			17	16	9	13	75				13	8	6	5	4	3
1 mo	8	5.1	1.26	11	5			11	5	7	8	77					7	5	4	4	3
1 yr	5	5.3	1.00	6	4			6	4	5	5	100							5		
Denver																					
5 min	114	6.4	1.93	73	63				70	73	63	73	69	58	44	26	14	9	7	5	2
1 hr	61	6.7	1.79	55	40				40	55	43	73		49	40	24	14	9	7	5	2
8 hr	37	6.9	1.66	30	27				27	29	30	74			29	18	12	9	7	6	3
1 day	28	7.1	1.60	20	16				16	20	20	76				16	11	9	7	6	4
1 mo	12	7.5	1.35	12	10				10	12	10	81					10	8	7	7	6
1 yr	8	7.9	1.00	8	7				7	8	8	100							7		
Los Angeles																					
5 min	72	9.5	1.58	81	70	81	70	75				79	81	50	36	25	16	12	10	9	7
1 hr	46	9.7	1.50	47	35	43	35	47				79		43	34	25	16	12	10	9	7
8 hr	32	9.9	1.43	28	27	28	28	27				81			27	21	15	12	10	9	8
1 day	26	10.0	1.39	23	22	22	22	23				82				19	15	12	11	9	8
1 mo	15	10.3	1.24	14	13	14	13	14				89					13	12	11	9	9
1 yr	11	10.6	1.00	11	9	11	9	11				100							11		
Philadelphia																					
5 min	83	6.7	1.77	67	43	51	52	43	67	47	44	58	65	48	35	21	13	9	7	5	3
1 hr	48	6.9	1.66	54	37	47	47	37	54	43	42	58		45	33	21	12	9	7	5	3
8 hr	31	7.1	1.56	36	23	36	35	27	26	34	23	59			27	19	12	8	7	5	3
1 day	24	7.2	1.50	25	14	23	25	21	19	20	14	60				18	11	8	7	5	4
1 mo	12	7.6	1.30	14	9		14	13	11	10	9	61					10	8	7	6	5
1 yr	8	7.9	1.00	8	6			7	6	7	6	67							7		

St. Louis																					
5 min	54	5.3	1.69	68	45			45	53	68	60	86	55	42	31	19	11	7	5	4	2
1 hr	32	5.5	1.59	29	25			25	27	29	27	86		27	23	17	11	7	5	4	2
8 hr	21	5.6	1.50	18	14			18	18	18	14	88			17	14	10	7	6	4	3
1 day	17	5.7	1.45	17	11			17	15	12	11	89				12	9	7	6	5	3
1 mo	9	5.9	1.27	9	8			9	9	8	8	94					8	7	6	5	5
1 yr	6	6.1	1.00	6	6			6	6	6	6	100							6		
San Francisco																					
5 min	39	4.7	1.62	40	38		38	40				67	38	27	20	14	9	6	5	4	2
1 hr	25	4.8	1.53	38	22		38	22				68		20	18	13	8	6	5	4	2
8 hr	17	4.9	1.46	18	14		18	14				68			13	11	8	6	5	4	3
1 day	14	5.0	1.41	14	10		14	10				69				9	7	6	5	4	3
1 mo	7	5.1	1.25	7	6		6	7				67					6	6	5	5	4
1 yr	5	5.3	1.00	5	5			5				50							5		
Washington																					
5 min	93	3.3	2.13	49	29	30	44	29	49	47	37	70				30	9	6	4	3	2
1 hr	46	3.5	1.95	41	25	25	41	28	32	38	32	70		35	28	17	8	5	4	3	2
8 hr	26	3.7	1.80	34	17	19	34	18	17	22	23	71			22	16	8	5	4	3	2
1 day	19	3.8	1.72	23	11	14	23	13	11	15	15	71				14	8	6	4	3	2
1 mo	7	4.2	1.42	10	5	7	10	6	6	5	7	75					7	5	4	4	3
1 yr	4	4.4	1.00	7	3		7	6	4	3	5	83							4		

Table 6–2. CARBON MONOXIDE CONCENTRATION BY AVERAGING TIME AND FREQUENCY, 1963 THROUGH 1967, IN CALIFORNIA
(ppm)

Location and averaging time	Calculated			Measured maxima		Maximum for year					% data avail	% of time concentration is exceeded:							
	Annl max	Geo mean	SGD	Max	Min	63	64	65	66	67		0.01	0.1	1	10	30	50	70	90
Anaheim																			
1 hr	36	5.4	1.64	35	18	18	26	26	35	35	94	12	25	15	9	7	6	5	3
8 hr	23	5.6	1.54	23	13	13	20	18	23	23	94		22	14	9	7	6	5	4
1 day	18	5.6	1.49	19	11	11	12	13	17	19	96			13	9	7	6	5	4
1 mo	9	5.9	1.30	10	6	6	7	8	8	10	98				8	7	6	6	5
1 yr	6	6.1	1.00	7	5	5	6	7	7	7	100						6		
Bakersfield																			
1 hr	24	2.2	1.87	23	12	12	17	19	23	22	81	19	15	10	4	3	2	1	1
8 hr	14	2.3	1.73	15	8	8	8	11	15	12	81		11	8	4	3	2	2	1
1 day	10	2.3	1.66	11	5	5	5	7	11	7	81			6	4	3	2	2	1
1 mo	4	2.5	1.39	4	3	3	3	4	4	4	84				3	3	2	2	1
1 yr	3	2.6	1.00	3	2		2	2	3	2	79						2		

Table 6–2 (continued). CARBON MONOXIDE CONCENTRATION BY AVERAGING TIME AND FREQUENCY, 1963 THROUGH 1967, IN CALIFORNIA (ppm)

Location and averaging time	Calculated			Measured Maxima		Maximum for year					% data avail	% of time concentration is exceeded:							
	Annl max	Geo mean	SGD	Max	Min	63	64	65	66	67		0.01	0.1	1	10	30	50	70	90
Fresno																			
1 hr	41	1.2	2.50	35	18	18	27	29	35	26	79	27	21	12	4	2	2	1	1
8 hr	19	1.4	2.23	18	13	13	15	18	15	16	79		15	10	4	2	2	1	1
1 day	13	1.4	2.09	9	5	5	8	9	7	7	79			6	4	2	2	1	1
1 mo	4	1.7	1.61	5	3	3	3	5	4	3	84				3	3	2	2	1
1 yr	2	1.9	1.00	2	2		2	2	2	2	79						2		
La Habra																			
1 hr	31	8.4	1.41	26	26					26	5	25	24	19	13	10	8	7	4
8 hr	23	8.5	1.35	20	20					20	7		18	16	12	10	9	7	4
1 day	19	8.5	1.32	15	15					15	7			14	11	0	9	7	5
1 mo	12	8.7	1.20	9	9					9	7				9	9	9	7	0
1 yr	9	8.9	1.00								0						9		
Oakland																			
1 hr	30	2.1	2.01	27	20	27	26	26	25	20	89	25	18	11	6	3	2	2	1
8 hr	16	2.2	1.84	16	12	12	14	16	12	12	91		12	10	6	4	3	2	1
1 day	12	2.3	1.75	11	9	9	10	10	11	9	91			9	5	4	3	2	1
1 mo	5	2.5	1.44	5	4	4	5	5	5	4	94				4	4	3	2	2
1 yr	3	2.7	1.00	4	3	3	3	4	3	3	100						3		
Port Chicago																			
1 hr	8	0.7	1.87	8	7				7	8	36	7	5	4	2	1	1	1	1
8 hr	5	0.8	1.73	4	4				4	4	36		4	3	2	2	1	1	1
1 day	3	0.8	1.66	3	3				3	3	36			3	2	1	1	1	1
1 mo	1	0.8	1.39	2	2				2	2	36				2	1	1	1	1
1 yr	1	0.9	1.00	1	1				1	1	41						1		
Redlands																			
1 hr	28	4.7	1.60	21	21					21	0	20	20	18	11	6	5	4	2
8 hr	19	4.8	1.51	15	15					15	0		14	14	11	6	5	4	3
1 day	15	4.9	1.46	13	13					13	0			10	7	6	5	4	4
1 mo	8	5.1	1.28	6	6					6	2				0	0	0	0	0
1 yr	5	5.2	1.00								0						0		
Redwood City																			
1 hr	15	3.3	1.48	15	15					15	14	13	11	8	5	4	3	3	2
8 hr	10	3.3	1.41	9	9					9	14		9	7	5	4	3	3	2
1 day	9	3.3	1.37	7	7					7	14			6	5	4	3	3	2
1 mo	5	3.4	1.23	4	4					4	14				4	3	3	3	3
1 yr	4	3.5	1.00	3	3					3	19						3		

Richmond																			
1 hr	26	2.1	1.92	25	13				13	25	22	21	16	10	5	3	2	1	1
8 hr	15	2.2	1.77	15	9				9	15	22		11	8	5	3	2	2	1
1 day	11	2.3	1.69	7	5				5	7	22			7	4	3	2	2	1
1 mo	4	2.5	1.41	4	3				3	4	24				4	3	3	2	1
1 yr	3	2.6	1.00	3	3					3	19						3		
Riverside																			
1 hr	26	3.9	1.65	74	15	17	15	24	17	74	77	22	18	13	8	5	4	2	1
8 hr	17	4.0	1.55	19	10	10	10	16	15	19	77		16	12	8	5	4	3	1
1 day	13	4.0	1.49	18	8	8	8	14	12	18	77			11	7	5	4	3	2
1 mo	7	4.2	1.30	8	4	4	5	6	6	8	89				6	5	4	3	2
1 yr	4	4.4	1.00	5	3	3	3	4	5	5	100						3		
Sacramento																			
1 hr	70	1.8	2.60	55	36	36	51	44	51	55	96	50	35	16	5	3	2	1	1
8 hr	31	2.0	2.31	39	24	24	30	31	28	39	96		28	13	5	3	2	1	1
1 day	21	2.1	2.16	17	12	12	14	15	13	17	96			11	4	3	2	2	1
1 mo	6	2.5	1.65	6	4	3	5	6	5	5	98				4	3	2	2	2
1 yr	3	2.9	1.00	3	2	2	3	3	2	3	100						2		
Salinas																			
1 hr	10	1.6	1.63	10	6				6	10	22	9	7	4	2	2	1	1	1
8 hr	7	1.6	1.53	5	4				4	5	22		5	4	2	2	1	1	1
1 day	5	1.6	1.48	3	2				2	3	22			3	2	2	1	1	1
1 mo	3	1.7	1.29	2	1				1	2	22				2	2	1	1	1
1 yr	2	1.7	1.00	1	1					1	19						1		
San Bernardino																			
1 hr	30	6.5	1.48	35	20	20	24	35	30	33	86	30	22	16	10	8	6	5	3
8 hr	21	6.6	1.41	22	15	18	15	22	19	21	86		19	15	10	8	6	5	3
1 day	17	6.7	1.37	16	11	13	11	15	16	16	86			13	10	8	7	5	3
1 mo	10	6.9	1.2[illegible]	10	6	6	6	10	10	10	94				9	8	6	6	4
1 yr	7	7.0	1.00	8	4	4	5	7	8	8	100						5		
San Diego																			
1 hr	48	1.9	2.32	45	26	33	38	45	37	26	81	34	26	15	6	3	2	1	0
8 hr	23	2.1	2.09	23	16	17	23	20	22	16	81		20	12	6	3	2	1	0
1 day	16	2.2	1.97	14	10	12	14	10	12	11	81			10	6	3	2	2	1
1 mo	5	2.5	1.55	8	3	5	8	6	3	5	84				5	3	3	2	1
1 yr	3	2.8	1.00	4	2	4	4	3	2	2	100						2		
San Francisco, Mission St																			
1 hr	34	2.9	1.91	38	27			27	27	38	55	34	21	12	6	4	3	2	1
8 hr	19	3.0	1.76	21	14			14	15	21	55		15	10	6	4	3	2	2
1 day	14	3.1	1.68	12	10			10	12	11	57			9	6	4	3	3	2
1 mo	6	3.3	1.40	6	5			5	5	6	57				5	4	3	3	2
1 yr	4	3.5	1.00	4	3			4	3	3	60						3		

Table 6–2 (continued). CARBON MONOXIDE CONCENTRATION BY AVERAGING TIME AND FREQUENCY, 1963 THROUGH 1967, IN CALIFORNIA (ppm)

Location and averaging time	Calculated			Measured Maxima		Maximum for year					% data avail	% of time concentration is exceeded:							
	Annl max	Geo mean	SGD	Max	Min	63	64	65	66	67		0.01	0.1	1	10	30	50	70	90
San Francisco, Union Square																			
1 hr	23	4.9	1.50	22	16	18	22	20			29	20	17	13	8	6	5	3	2
8 hr	16	5.0	1.43	17	13	17	13	16			29		13	11	8	6	5	4	2
1 day	13	5.0	1.39	14	9	14	9	9			29			9	7	6	5	4	3
1 mo	7	5.2	1.24	6	6	6	6	6			31				6	5	5	4	4
1 yr	5	5.3	1.00	5	5		5				19						5		
San Jose																			
1 hr	30	2.9	1.83	29	19	19	27	20	20	29	79	25	19	13	7	4	3	2	1
8 hr	17	3.0	1.70	19	14	14	19	14	14	15	81		15	11	7	4	3	2	1
1 day	13	3.1	1.63	13	7	7	13	12	10	10	81			10	6	4	3	2	2
1 mo	6	3.3	1.37	7	3	3	6	7	5	5	84				5	4	3	3	2
1 yr	4	3.5	1.00	5	3		4	5	3	3	79						3		
San Rafael																			
1 hr	24	2.2	1.87	17	17					17	2	15	15	12	6	3	2	2	1
8 hr	14	2.3	1.73	7	7					7	2		7	6	5	4	3	2	2
1 day	10	2.3	1.66	5	5					5	2			5	4	4	3	3	2
1 mo	4	2.5	1.39	3	3					3	2				3	3	3	3	0
1 yr	3	2.6	1.00								0						3		
Santa Ana Airport																			
1 hr	14	6.3	1.23	15	15					15	7	14	12	10	8	7	6	6	5
8 hr	12	6.3	1.20	11	11					11	7		10	9	8	7	6	6	5
1 day	11	6.3	1.18	10	10					10	7			9	8	7	6	6	5
1 mo	8	6.4	1.12	7	7					7	7				7	7	6	6	0
1 yr	6	6.4	1.00								0						6		
Santa Barbara																			
1 hr	39	2.0	2.17	31	26		26	31	28		46	20	22	14	5	3	2	2	1
8 hr	20	2.1	1.98	19	12		12	15	19		48		15	11	5	3	3	2	2
1 day	14	2.2	1.87	9	8		9	8	9		48			8	5	3	3	2	2
1 mo	5	2.5	1.50	5	5		5	5	5		48				4	4	3	2	2
1 yr	3	2.7	1.00	3	3		3	3			41						3		
Santa Cruz																			
1 hr	4	0.8	1.53	4	4				4	4	22	4	3	3	2	1	1	1	1
8 hr	3	0.8	1.46	3	3				3	3	22		3	3	2	1	1	1	1
1 day	2	0.8	1.41	2	2				2	2	22			2	2	1	1	1	1
1 mo	1	0.9	1.25	2	1				2	1	24				1	1	1	1	1
1 yr	1	0.9	1.00	1	1					1	19						1		

Stockton																		
1 hr	24	1.3	2.13	35	15	16	23	21	15	35	86	22	14	8	3	2	1	1	0
8 hr	13	1.4	1.94	19	7	8	14	11	7	19	86		11	7	3	2	1	1	0
1 day	9	1.5	1.84	13	4	5	7	6	4	13	86			5	3	2	1	1	1
1 mo	3	1.7	1.49	4	2	2	3	3	2	4	91				2	2	1	1	1
1 yr	2	1.8	1.00	2	1		2	2	1	2	79						2		
Upland APCD																			
1 hr	28	3.0	1.80	28	26				26	28	22	26	18	12	6	4	3	2	1
8 hr	17	3.1	1.67	12	12				12	12	22		12	10	6	4	3	3	2
1 day	13	3.1	1.60	8	8				8	8	22			8	5	4	3	3	2
1 mo	6	3.3	1.36	5	5				5	5	24				5	4	3	3	2
1 yr	4	3.5	1.00	3	3					3	19						3		
Ventura																			
1 hr	14	1.5	1.80	13	12		12	13	12		48	12	9	5	3	2	2	2	1
8 hr	8	1.5	1.67	6	6		6	6	6		48		6	4	3	2	2	2	1
1 day	6	1.6	1.60	4	4		4	4	4		48			4	3	2	2	2	1
1 mo	3	1.7	1.36	3	2		3	3	2		50				3	2	2	2	2
1 yr	2	1.8	1.00	2	2		2	2			41						2		

Table 6–3. CARBON MONOXIDE CONCENTRATION BY AVERAGING TIME AND FREQUENCY, 1956 THROUGH 1967, IN LOS ANGELES COUNTY
(ppm)

Location and averaging time	Calculated			Measured maxima		Maximum for year												% data avail	% of time concentration is exceeded:							
	Annl max	Geo mean	SGD	Max	Min	56	57	58	59	60	61	62	63	64	65	66	67		0.01	0.1	1	10	30	50	70	90
Avalon Village																										
1 hr	40	9.0	1.48	37	28			28	37	35	36	32						35	34	30	23	15	11	9	8	7
8 hr	28	9.1	1.41	29	24			24	27	29	27	28						36		27	22	14	11	9	9	7
1 day	24	9.2	1.37	23	14			14	18	23	21	19						36			18	13	11	10	9	8
1 mo	13	9.5	1.23	14	11			11	13	14	14	13						37				13	11	10	9	8
1 yr	10	9.7	1.00	11	9			9	10	11	11	10						42						10		
Azusa, 803 Loren																										
1 hr	23	8.8	1.28	27	11		11	18	27	18	22	24	27	25	20	19	21	81	23	19	15	12	10	8	7	4
8 hr	18	8.8	1.25	23	8		8	12	22	16	20	18	23	17	16	18	18	82		18	15	12	10	9	7	4
1 day	16	8.9	1.22	20	7		7	8	15	15	17	15	20	15	16	14	16	83			14	12	10	9	7	4
1 mo	11	9.0	1.14	12	5		5	5	10	10	12	11	11	10	11	12	12	85				11	10	9	8	4
1 yr	9	9.1	1.00	11	4		4	4	9	8	9	10	9	8	9	9	11	92						9		
Azusa, 827 N Azusa																										
1 hr	18	5.1	1.39	17	16	16	17											9	16	14	11	7	6	5	4	3
8 hr	13	5.1	1.34	13	12	13	12											9		12	10	7	6	5	4	3
1 day	11	5.2	1.30	9	8	8	9											9			8	7	6	5	4	3
1 mo	7	5.3	1.19	6	6	6	6											10				6	5	5	4	4
1 yr	5	5.3	1.00	5	5	5												8						5		

Table 6–3 (continued). CARBON MONOXIDE CONCENTRATION BY AVERAGING TIME AND FREQUENCY, 1956 THROUGH 1967, IN LOS ANGELES COUNTY
(ppm)

Location and averaging time	Calculated			Measured maxima		Maximum for year												% data avail	% of time concentration is exceeded:							
	Annl max	Geo mean	SGD	Max	Min	56	57	58	59	60	61	62	63	64	65	66	67		0.01	0.1	1	10	30	50	70	90
Burbank, 1508 Burbank																										
1 hr	69	6.5	1.85	56	41	41	43	42	43	51	56							43	53	44	29	15	9	7	5	3
8 hr	40	6.8	1.72	47	31	33	35	31	32	40	47							44		37	26	14	9	7	5	3
1 day	30	7.0	1.65	26	18	18	22	21	20	26	26							44			21	13	9	7	6	4
1 mo	13	7.5	1.38	16	12	12	13	13	14	15	16							47				12	9	7	6	4
1 yr	8	7.9	1.00	11	5	5	7	8	9	11	9							50						8		
Burbank, 228 W Palm																										
1 hr	60	11.2	1.55	68	30						30	60	68	54	40	39	42	48	54	43	29	18	14	13	11	9
8 hr	40	11.4	1.47	50	25						25	50	50	42	33	31	31	48		37	27	18	14	13	11	9
1 day	33	11.5	1.42	29	18						18	23	29	28	27	24	25	49			24	17	15	13	12	10
1 mo	18	12.0	1.26	21	9						9	14	17	21	17	19	17	50				16	14	13	12	10
1 yr	12	12.3	1.00	15	12							12	14	13	14	15	12	50						13		
Downey, Ranch Los Amigos																										
1 hr	40	9.0	1.48	40	35				35	37	35	40						26	35	30	23	15	11	10	9	7
8 hr	28	9.1	1.41	27	24				25	27	24	27						26		25	20	14	11	10	9	7
1 day	24	9.2	1.37	21	17				17	18	20	21						26			17	13	11	10	9	8
1 mo	13	9.5	1.23	13	13				13	13	13	13						26				13	11	10	10	9
1 yr	10	9.7	1.00	11	9				9	11	11							25						9		
El Monte, 2720 Peck																										
1 hr	36	3.7	1.81	29	27	27	29											12	28	23	15	8	5	4	3	2
8 hr	21	3.8	1.68	20	18	18	20											12		17	13	8	6	4	4	2
1 day	16	3.9	1.61	15	12	15	12											12			11	8	5	5	4	3
1 mo	7	4.2	1.36	8	7	8	7											13				7	5	4	4	3
1 yr	4	4.4	1.00	5	4	5	4											17						4		
El Segundo, 301 Coast																										
1 hr	18	5.1	1.39	16	13		13	16										8	16	14	11	8	6	6	5	4
8 hr	13	5.1	1.34	13	11		11	13										8		12	10	8	6	6	5	4
1 day	11	5.2	1.30	10	9		9	10										8			9	8	6	6	5	4
1 mo	7	5.3	1.19	7	7		7	7										9				7	6	6	6	4
1 yr	5	5.3	1.00	6	6			6										8						6		
Florence, Roosevelt Park																										
1 hr	45	7.9	1.57	43	32					32	42	43						15	42	32	23	13	10	8	7	5
8 hr	30	8.1	1.49	31	20					20	26	31						15		27	19	13	10	9	7	5
1 day	24	8.2	1.44	25	13					13	19	25						15			17	12	10	9	7	5
1 mo	13	8.5	1.27	13	10					10	12	13						17				11	10	9	9	5
1 yr	9	8.8	1.00	10	7						7	10						17						7		

Hollywood Freeway																										
1 hr	53	11.4	1.49	50	42								48	45	42	50	50	33	48	39	29	19	14	12	10	8
8 hr	37	11.6	1.42	38	33								35	33	33	36	38	34		35	26	18	14	12	10	9
1 day	30	11.7	1.38	26	21								21	22	24	26	26	34			22	18	15	13	11	9
1 mo	17	12.1	1.23	18	14								14		18	18	18	35				17	14	13	11	9
1 yr	12	12.3	1.00	15	11								11		15	14	14	42						12		
Inglewood, 5037 W Imperl																										
1 hr	57	13.1	1.47	48	31							31	48	47	47			17	48	43	33	21	16	13	11	9
8 hr	41	13.3	1.40	40	24							24	39	40	34			17		36	29	20	16	14	12	9
1 day	34	13.4	1.36	29	17							17	27	29	26			18			25	20	16	14	12	10
1 mo	19	13.8	1.22	20	13							13	17	20	20			18				19	15	13	13	10
1 yr	14	14.1	1.00	15	12								12	15				17						12		
Lennox, 4380 Lennox																										
1 hr	66	11.9	1.56	56	42	42	48	56										18	55	47	35	21	15	12	8	5
8 hr	44	12.2	1.48	47	31	31	40	47										19		40	32	20	15	12	8	5
1 day	36	12.3	1.43	35	21	21	34	35										19			27	20	16	12	8	6
1 mo	19	12.8	1.26	21	13	13	21	21										20				19	16	12	9	6
1 yr	13	13.1	1.00	15	8	8	15											17						8		
L A, Pirshing Square																										
1 hr	62	7.5	1.73	58	44	44	54	58	52									20	52	41	27	14	10	8	6	4
8 hr	38	7.8	1.62	32	27	31	32	27	32									21		31	23	13	10	8	7	5
1 day	29	7.9	1.56	24	18	18	21	20	24									21			18	13	10	8	7	5
1 mo	14	8.4	1.33	14	11	11	13	11	14									21				11	9	8	7	6
1 yr	9	8.7	1.00	9	8		8	9										17						8		
L A, 434 S San Pedro																										
1 hr	49	8.7	1.57	60	37	38	41	47	55	50	57	63	42	47	37	38	40	86	47	35	25	15	11	9	8	6
8 hr	33	8.9	1.49	32	21	21	23	26	30	27	28	32	31	26	28	27	26	87		27	22	15	12	10	8	6
1 day	26	9.0	1.44	26	14	14	14	18	22	21	23	26	21	22	22	20	21	88			19	14	12	10	8	6
1 mo	14	9.4	1.27	16	9	9	10	11	14	13	13	14	15	14	16	14	12	91				13	11	10	9	7
1 yr	10	9.6	1.00	13	6	6	8	8		11	10	11	11	11	13	10	10	92						10		
L A, USC Medical Center																										
1 hr	40	10.9	1.40	40	32							32	38	38	40	35	32	47	37	31	24	16	13	12	10	9
8 hr	29	11.0	1.35	29	25							28	29	29	28	25	26	47		26	22	16	13	12	11	9
1 day	25	11.1	1.31	22	19							22		22	22	20	19	48			20	16	13	12	11	9
1 mo	15	11.4	1.19	18	13							14		17	18	15	13	49				15	13	12	11	10
1 yr	12	11.5	1.00	13	11							11		13	13	12	12	50						12		
North Long Beach																										
1 hr	38	11.0	1.18	37	25							25	35	37	34	33	33	40	34	30	25	17	13	12	11	9
1 hr	29	11.1	1.33	28	20							20	28	28	27	26	26	41		26	23	17	14	12	11	10
1 day	24	11.2	1.30	24	17							17	23	24	23	22	22	41			21	16	14	12	11	10
1 mo	15	11.4	1.19	18	13							13	14	17	18	16	15	42				15	13	12	11	10
1 yr	12	11.6	1.00	14	12								12	14	14	13	12	42						12		

Table 6–3 (continued). CARBON MONOXIDE CONCENTRATION BY AVERAGING TIME AND FREQUENCY, 1956 THROUGH 1967, IN LOS ANGELES COUNTY
(ppm)

Location and averaging time	Calculated			Measured maxima		Maximum for year												% data avail	% of time concentration is exceeded:							
	Annl max	Geo mean	SGD	Max	Min	56	57	58	59	60	61	62	63	64	65	66	67		0.01	0.1	1	10	30	50	70	90
Pasadena, Memorial Park																										
1 hr	41	8.0	1.13	40	27	27	40	34										21	40	30	20	13	10	8	6	4
8 hr	28	8.2	1.46	27	19	19	27	20										22		21	17	12	10	8	7	5
1 day	23	8.3	1.41	17	15	15	16	17										22			14	11	10	8	7	6
1 mo	12	8.6	1.25	11	9	9	10	11										22				10	9	9	7	6
1 yr	9	8.8	1.00	10	7	7	9	10										25						7		
Pasadena, 862 Villa																										
1 hr	46	9.7	1.30	48	36			40	48	40	38	37	37	40	41	38	36	70	40	34	26	17	12	11	9	7
8 hr	32	9.9	1.13	34	26			31	34	30	29	26	32	30	33	29	26	71		29	23	16	12	11	10	8
1 day	26	10.0	1.09	25	19			20	22	23	25	20	25	24	22	19	20	72			20	15	12	11	10	8
1 mo	15	10.3	1.24	18	11			12	14	18	15	14	17	11	13	13	13	73				13	12	11	10	9
1 yr	11	10.6	1.00	13	10				12	12	11	11	13	10	11	11	11	75						11		
Pomona, 924 N Garey																										
1 hr	26	11.7	1.23	30	23										25	30	23	20	24	22	18	14	13	12	11	10
8 hr	21	11.7	1.20	22	18										22	18	19	20		18	17	14	13	12	11	11
1 day	19	11.8	1.18	16	16										16	16	16	20			15	14	13	12	11	11
1 mo	14	11.9	1.11	13	13										13	13	13	20				13	12	12	12	11
1 yr	12	11.9	1.00	12	12											12	12	17						12		
Lennox, 11408 Lacienga																										
1 hr	61	14.9	1.44	59	51										57	59	51	23	55	46	36	23	18	15	11	9
8 hr	43	15.1	1.38	42	34										39	42	34	23		39	33	23	18	15	12	10
1 day	37	15.2	1.34	35	29										32	35	29	23			30	22	18	15	12	10
1 mo	22	15.6	1.21	26	17										25	26	17	24				22	17	15	13	10
1 yr	16	15.9	1.30	19	12										19	16	12	25						12		
Reseda, 18330 Gault																										
1 hr	53	11.4	1.49	44	43										43	44	44	22	43	39	28	17	14	12	10	9
8 hr	37	11.6	1.42	36	34										34	35	35	22		34	26	17	14	12	11	9
1 day	30	11.7	1.38	24	22										22	24	24	23			22	16	14	12	11	9
1 mo	17	12.1	1.23	17	14										14	14	17	22				15	14	12	11	10
1 yr	12	12.3	1.00	14	11										13	11	14	25						11		
Reseda, 19630 Sherman																										
1 hr	25	4.8	1.53	20	20	20												6	20	18	13	8	6	5	4	3
8 hr	17	4.9	1.46	15	15	15												6		14	12	8	6	5	4	3
1 day	14	5.0	1.41	10	10	10												6			10	7	6	5	4	3
1 mo	7	5.1	1.25	7	7	7												6				6	5	5	5	4
1 yr	5	5.3	1.00	5	5	5												8						5		

Rivera, 8841 E Slauson																										
1 hr	38	5.4	1.67	40	23	33	31	40	23									24	33	26	18	10	7	5	4	3
8 hr	24	5.5	1.57	23	18	18	19	23	19									24		19	16	9	6	5	4	3
1 day	19	5.6	1.51	18	9	9	12	18	11									24			12	8	7	6	5	3
1 mo	9	5.9	1.31	9	6	6	8	9	6									26				8	6	5	5	4
1 yr	6	6.1	1.00	7	5	5	6	7										25						5		
Torrance, 1657 Gramercy																										
1 hr	34	5.5	1.62	34	27	31	27	34										18	31	24	18	11	7	6	5	3
8 hr	22	5.6	1.52	23	18	18	20	23										18		19	15	10	8	6	5	4
1 day	18	5.7	1.47	16	13	13	14	16										19			13	10	8	6	5	4
1 yr	9	5.9	1.29	10	7	7	9	10										19				9	7	6	5	4
1 yr	6	6.1	1.00	7	5	5	7											17						5		
Vernon, 5201 Santa Fe																										
1 hr	42	4.4	1.30	40	26	26	31	40	38									25	35	27	18	10	6	5	4	3
8 hr	25	4.6	1.67	24	17	17	23	19	24									26		21	16	9	7	5	4	3
1 day	19	4.7	1.60	19	12	12	19	15	17									26			14	9	7	5	4	3
1 mo	8	5.0	1.36	11	7	7	11	8	8									27				8	6	6	5	4
1 yr	5	5.3	1.00	6	5	5	6	6										25						5		
West L A, 844 S La Brea																										
1 hr	64	8.3	1.70	61	34		34	55	58	61	58	48						40	55	43	28	15	11	9	7	5
8 hr	40	8.6	1.69	41	22		22	37	33	41	36	37						40		36	25	15	11	9	8	6
1 day	31	8.8	1.63	28	14		14	21	25	28	25	25						40			22	14	11	9	8	6
1 mo	15	9.2	1.32	16	9		9	10	14	15	14	16						42				14	11	9	8	7
1 yr	10	9.6	1.00	13	7			7	9	10	11	13						42						9		
West L A, 4409 W Pico																										
1 hr	63	5.8	1.87	48	47	48	47											14	48	40	26	13	8	6	5	4
8 hr	37	6.0	1.13	35	31	35	31											14		31	21	12	8	7	6	4
1 day	28	6.2	1.66	22	18	18	22											14			16	12	9	7	6	5
1 mo	11	6.7	1.39	12	10	10	12											15				10	8	7	6	5
1 yr	7	7.0	1.00	8	7	8	7											17						7		
West L A, 2351 Westwood																										
1 hr	50	10.5	1.50	52	11							11	48	45	38	52	45	40	47	37	26	17	13	11	10	8
8 hr	35	10.7	1.43	41	10							10	34	29	28	41	32	40		32	23	16	13	11	10	8
1 day	29	10.8	1.39	25	20								25	21	22	24	20	41			20	16	13	12	10	9
1 mo	16	11.2	1.24	16	12								15	13	16	16	12	42				14	13	12	11	10
1 yr	11	11.4	1.00	13	10								12	11	13	13	10	42						11		

NOTE: The Los Angeles County Air Pollution Control District estimates that its reported concentration of carbon monoxide prior to April, 1968 at all locations in Los Angeles County are from 1 to 4 ppm high because of water vapor interference; the actual amount in this range is dependent on the absolute humidity at the time of measurement.

Table 6–4. CARBON MONOXIDE CONCENTRATION BY AVERAGING TIME AND FREQUENCY, FROM DECEMBER 1, 1961, TO DECEMBER 1, 1967, CHICAGO CAMP STATION
(ppm)

Averaging time	Annl arith mean	Max	Min	% data avail	% of time concentration is exceeded:																
					0.001	0.01	0.1	1	10	20	30	40	50	60	70	80	90	99	99.9	99.99	99.999
5 min	12	78	0	53	69	58	45	34	22	18	16	13	11	10	8	6	4	0	0	0	0
10 min	12	75	0	54		57	43	33	22	18	16	14	12	10	8	6	4	0	0	0	
15 min	12	69	0	54		56	42	32	22	18	16	14	12	10	8	6	4	0	0	0	
30 min	12	63	0	54		55	41	32	22	18	16	14	12	10	8	6	4	0	0	0	
1 hr	12	59	0	54		54	41	31	22	18	16	14	12	10	8	6	4	1	0	0	
2 hr	12	52	0	53			38	30	22	18	16	14	12	10	8	6	4	1	0		
4 hr	12	51	0	54			36	29	21	18	16	14	12	10	8	6	4	1	0		
8 hr	*12*	*44*	*0*	*55*			*35*	*27*	*21*	*18*	*16*	*14*	*12*	*10*	*8*	*7*	*5*	*1*	*0*		
12 hr	12	39	0	55				26	21	18	15	14	12	10	8	7	5	1			
1 day	12	33	0	55				25	20	18	15	13	12	10	8	7	5	2			
2 day	12	30	2	52				24	20	17	15	14	12	10	9	7	6	3			
4 day	12	27	3	54					19	17	15	13	11	10	9	8	6				
7 day	12	24	3	56					19	17	15	13	11	10	9	8	6				
14 day	12	23	5	59					19	17	15	14	11	10	9	8	7				
1 mo	12	21	6	60					18	16	15	13	11	10	9	7	7				
2 mo	13	21	7	58						17	14	13	11	11	9	8					
3 mo	12	20	7	63						15	14	13	11	11	9	8					
6 mo	12	19	8	58						14	12	12	10	9	9	8					
1 yr	14	17	12	50									12								

used to describe aerometric measurements: (2) to suggest a means of organizing the data in order to arrive at the aforementioned parameters; and (3) to present an air quality model that makes use of these parameters and statistical considerations to extract as much information as possible from the data at hand.

b. Averaging Time

The air quality of an area is estimated by analysis of the pollutant concentrations taken at specific locations over a selected period of time. Each recorded measurement of concentration is indicative both of the absolute magnitude of the actual concentration and of the response time of the instrument. Because of the response time of the instrument, any single recorded concentration is of necessity an average concentration over the time interval of the measurement.

Reported CO measurements are based on either spot or integrated measurements taken over a variety of sampling time periods. It is necessary to arrive at a uniform averaging time because of two basic considerations:

1. The need to compare concentrations measured at different sampling sites.
2. The need to select an averaging time meaningful to the effects produced by the pollutant.

The minimum averaging time is an inflexible parameter of the particular instrument used, but the resulting data may be reported on the basis of any averaging time equal to or greater than this minimum value. For example, while the nondispersive infrared CO analyzer (NDIR), used in the CAMP network, senses and measures on a continuous basis, it only records an instantaneous measurement once every 5 minutes. The 12 consecutive 5-minute measurements within an hour may then be averaged to give the 1-hour averaging time value.

An averaging time of 8 hours is frequently used for the presentation of CO concentrations. At low atmospheric CO concentrations, such as those found in community air, from 4 to 12 hours is required for the carboxyhemoglobin levels in the human body to reach equilibrium with the average concentration of CO being inspired. Because of the slow absorption and desorption of CO at these low levels by man, short-term concentrations are of less interest than this 8-hour average-value.

c. Frequency Distribution

Use of a frequency distribution is a common method of reducing a set of data of consistent averaging time. The advantage in using such a technique is that it automatically attaches an estimate of the probability of occurrence to any single measurement. This feature is important in assessing the severity of pollution. Moreover, certain frequency distributions have been well studied and lend themselves to statistical analysis. The frequency distribution of the available data can then be used to determine whether one of these common distributions may be fitted, thereby facilitating the extraction of statistical parameters of the data.

Most samples of atmospheric pollution concentrations have been found to exhibit a log-normal frequency distribution. Simply stated, this implies that the logarithms of the concentrations have a gaussian (normal) distribution; therefore, the wealth of statistical techniques used with normally distributed data may be applied as well to the logarithms of aerometric data.

One such technique is the use of probability graph paper to graphically depict a distribution under consideration. When the cumulative frequency distribution of a collection of air quality measurements is plotted on log-versus-normal-probability paper, the resulting curve can usually be approximated by a straight line. The concentration at the 50 percent mark, representing the arithmetic median value, is termed the geometric mean. Theoretically, half of the time measured concentrations will be below this value and half of the time they will be above it.

For a log-normal distribution, the geometric mean is a measure of central tendency. Similarly, the 84.13 percentile value divided by the 50.00 percent value (geometric mean) is termed the standard geometric deviation and is a measure of the dispersion of the data. Knowing these two values permits determination of the entire distribution.

The arithmetic mean of log-normally-distributed air-quality measurements is always larger than the geometric mean. The arithmetic mean, m, may be calculated[16] from the geometric mean, Mg, and standard geometric deviation (σ_g), by means of the following equation:

$$\log m = \log M_g + 1.151 (\log \sigma_g)^2$$

All of the CAMP data for the periods 1962 through 1967 inclusive have been analyzed to give concentration as a function of averaging time and frequency. Examples of the types of summaries that may be extracted from these data are shown in Tables 6–1 and 6–4, and Figure 6–6.

Table 6–4 shows a summary of 5-minute CO concentrations measured continuously for 6 years in Chicago. As indicated in the table, the 8-hour-averaging-time concentrations of CO from 5-minute values measured at the CAMP site in Chicago from December 1, 1961, to December 1, 1967, had an arithmetic mean of 14 mg/m^3 (12 ppm), a maximum of 51 mg/m^3 (44 ppm), and a minimum of 0 mg/m^3 (0 ppm). Data were available for 55 percent of all the 8-hour periods. The 8-hour-averaging-time measured concentrations exceeded 24 mg/m^3 (21 ppm) for 10 percent of all the 8-hour periods for which values were available and exceeded 14 mg/m^3 (12 ppm) half of the time (50 percentile).

Table 6–1, prepared by using a similar analysis, presents comparable data for the entire CAMP network.

It is evident by proceeding down the percentile columns in Table 6–4 or by reference

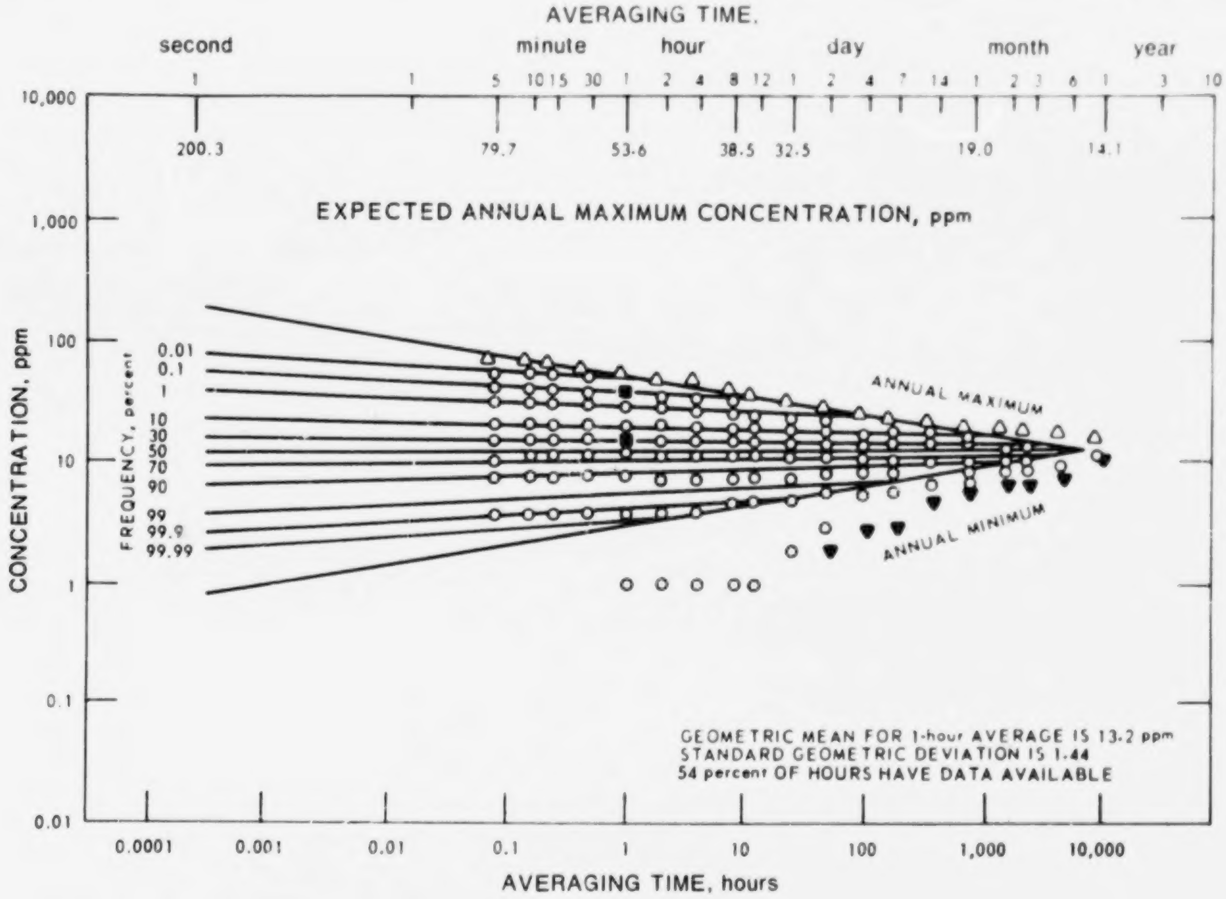

Figure 6-6. Concentration versus averaging time and frequency for carbon monoxide from December 1, 1961, to December 1, 1967, Chicago CAMP station.

to Figure 6–6 that the magnitude of concentrations greater than the geometric mean tend to decrease with an increase in averaging time whereas the magnitude of concentrations less than the geometric mean tend to increase with an increase in averaging time. Similarly, the geometric mean concentration for any averaging time tends to remain relatively constant. These trends are inherent in the averaging process and result in a decrease in the dispersion of the concentration values as the time over which these concentrations are averaged increases. As would be expected, this decrease in dispersion is reflected in a decrease of standard geometric deviation with increasing averaging time.

d. An Air Quality Model

Certain trends become apparent when the frequency of occurrence of various CO concentrations and their variability with averaging time are examined. In an extensive analysis of urban pollution data, Larsen[17] has found that:

1. Concentrations are approximately log-normally distributed for CO and other pollutants in all cities for all averaging times.
2. The median concentration (50th percentile) is proportional to the averaging time raised to an exponent.

These two factors greatly simplify the analysis of aerometric data. The former implies a common form of distribution of concentrations, independent of geographic location and amenable to statistical analysis. Such a distribution plots as a straight line on a log-versus-probability scale; therefore the distribution may be defined by relatively few points. The latter factor implies that once the distribution of concentrations for one averaging time is known, distributions for other averaging times may then be calculated.

These characteristics of the measurement data have been used to build a statistical model expressing air pollutant concentration as a function of averaging time and frequency. The accuracy of this model in depicting the expected air quality of a region depends on certain characteristics of the sampling data input; the larger the sample and the closer the sample data to meeting the two conditions cited above, the more accurately will the model simulate reality. (Because of the strong dependence of this model on the assumption of log normality and the ease with which a data set may be checked for exhibition of a log-normal distribution, i.e., the use of the log-versus-normal-probability paper, it is wise to check any data set against this assumption before applying the model.)

Two values of air quality, the 1-hour-averaging-time concentration that is exceeded 0.1 percent of the time and the 1-hour-averaging-time concentration that is exceeded 30 percent of the time, are used to produce a model that best depicts the most polluted half of the air samples, which are of greatest interest. One-hour averaging times are used because the model is general for gaseous air pollutants and the response times for some air-sampling instruments (such as those for nitrogen oxides) may be as long as a half hour (thus causing errors in concentration measurements averaged over less than 1 hour). Another reason is that more data averaged over 1 hour are available than for any other averaging period.

3. Eight-hour 0.1 Percentile Averages

In the CO data to follow, the concentrations listed are those that were exceeded at a particular sampling site 0.1 percent of the time. There are 1095 discrete 8-hour periods contained in a year; therefore, the 0.1 percentile value approximates the 8-hour-averaging-time concentration likely to be exceeded an average of once a year. This value then represents an estimate of the highest 8-hour exposure to which an individual would be subjected in a particular community annually. The sampling year was chosen to begin at midnight on December 1.

a. CAMP Observations

Figure 6–7 depicts the 0.1 percentile 8-hour-averaging-time CO concentrations recorded at CAMP sites throughout the Nation. These stations, which use similar measurement techniques, are located in the

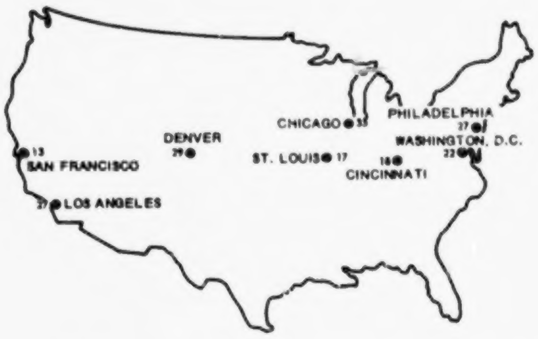

Figure 6-7. Eight-hour-averaging-time carbon monoxide concentrations (ppm) exceeded 0.1 percent of the time at CAMP sites, 1962 through 1967.

central business area from 10 to 100 feet from the edge of the street, depending on local considerations. The values depicted in Figure 6–7 range from 15 mg/m^3 (13 ppm) in San Francisco to 40 mg/m^3 (35 ppm) in Chicago and are, on the average, 3.4 times the median (geometric mean) concentrations recorded at these sites.

Maximum air pollutant concentrations within a community (including CO) may vary markedly from year to year. The maximum measured in one year in a particular community may be twice the maximum measured in another year. This is the case, for instance in Chicago, Cincinnati, and Washington (Table 6–1), where the maximum 8-hour concentration measured in each of these cities in the most polluted year is about twice the maximum concentration measured in the cleanest year. The developed statistical model has been used to calculate the maximum concentration predicted to occur on the average of once a year, i.e., the calculated annual maximum 8-hour concentration. For any averaging time, although observed year-to-year mean and peak CO values may vary markedly within any community, the calculated annual maximum value remains constant.

b. California Observations

Continuous air monitoring networks have been operated by the State of California and by the County of Los Angeles for a number of years. The localized patterns of CO concentration that have been observed and measured on a continuous basis in these two networks reveal the CO variability from time to time and place to place. Using an analysis similar to that used for the CAMP data in Table 6–1, comparable information is presented for the State of California in Table 6–2. The values for 8-hour-averaging time CO concentrations that are exceeded 0.1 percent of the time at various California sites are plotted in Figure 6–8.

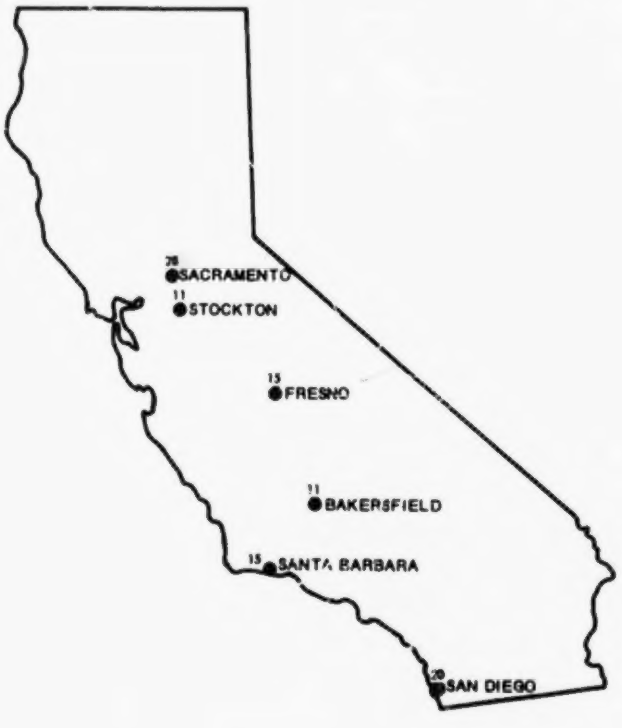

Figure 6-8. Eight-hour-averaging-time carbon monoxide concentrations (ppm) exceeded 0.1 percent of the time at various California sites, 1963 through 1967.

Similar data from the Los Angeles Area are given in Table 6–3 and shown in Figure 6–9. The concentration range displayed in Figure 6–9 is from 12 to 46 mg/m^3 (10 to 40 ppm).

As noted at the end of Table 6–3, Los Angeles County estimates that water vapor contributed up 5 mg/m^3 (4 ppm) of their measured carbon monoxide concentrations. This water vapor interference is a function of

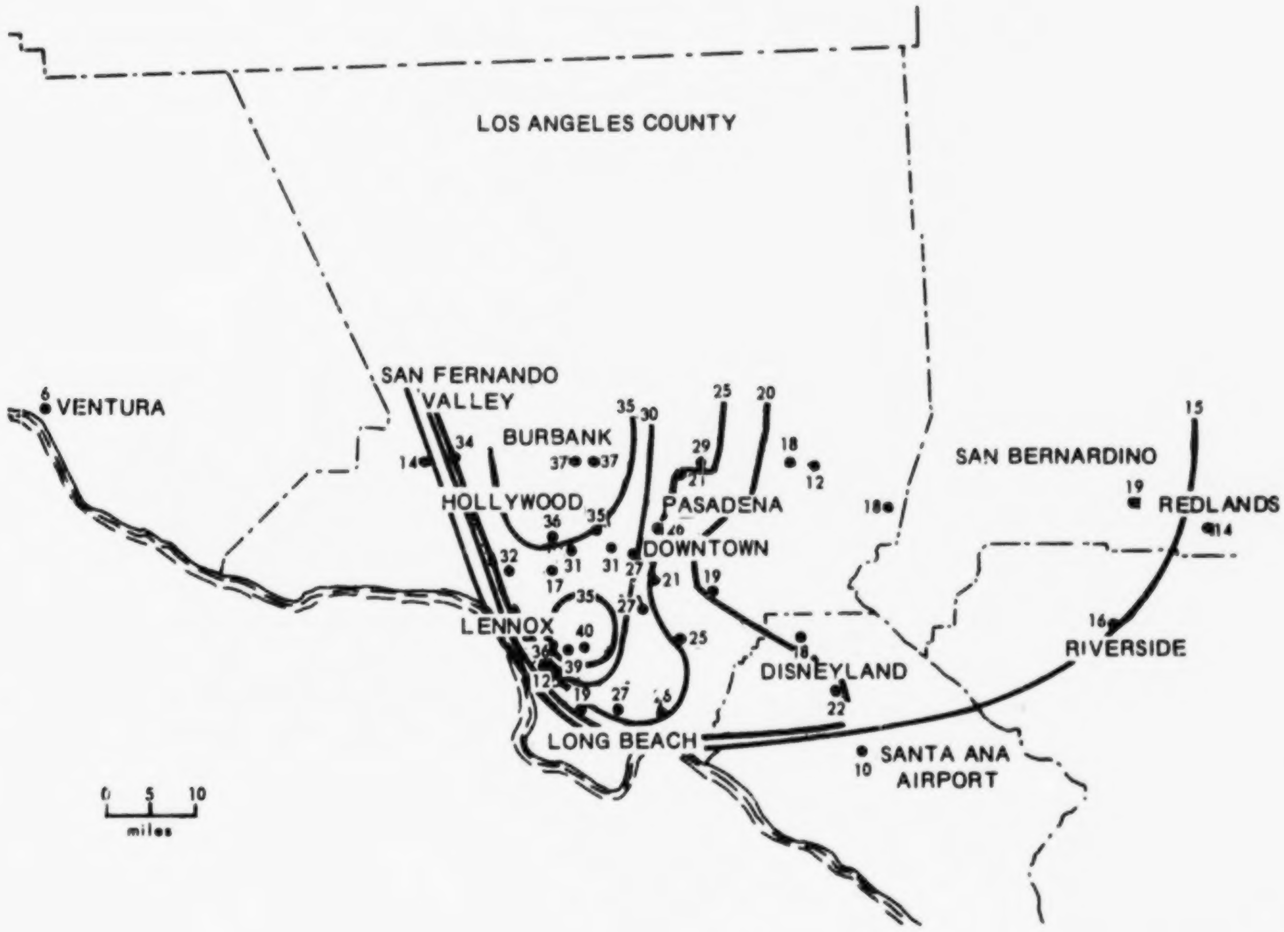
LOS ANGELES COUNTY
6
VENTURA
SAN FERNANDO VALLEY
BURBANK
37
37
14
34
35
30
25
20
29
21
18
12
HOLLYWOOD
36
35
PASADENA
26
DOWNTOWN
18
SAN BERNARDINO
19
REDLANDS
14
15
32
31
17
31
27
21
19
35
27
40
36
39
12
19
27
16
25
18
DISNEYLAND
22
LENNOX
LONG BEACH
16
RIVERSIDE
10
SANTA ANA AIRPORT
0
5
10
miles

Figure 6-9. Eight-hour-averaging-time carbon monoxide concentrations (ppm) exceeded 0.1 percent of the time in Los Angeles area, 1956 through 1967.

the absolute humidity, as was discussed in Chapter 5. Considering the humidity range in the Los Angeles area, it would be expected, on the basis of the curve shown in Figure 5–1, that water vapor interference would be on the order of up to 12 mg/m^3 (10 ppm) rather than the stated 1 to 5 mg/m^3 (1 to 4 ppm.) This later expectation cannot be checked, however, with any degree of certainty because the water vapor interference study depicted in Figure 5–1 was not determined with Los Angeles County instruments. Nevertheless, it is important to recognize that water vapor was affecting the reported CO values for Los Angeles County prior to April, 1968. Since that time, the instruments have been modified to eliminate this interference.

4. Special Carbon Monoxide Exposure Situations

a. Variations with Type of Vehicle Traffic

Larsen and Burke[18] have recently analyzed, using the frequency distribution described earlier, aerometric CO data from a variety of sampling locations in many cities. These studies included data from various cities of the continuous air monitoring networks, commuter traffic surveys, and special studies. The data were treated so as to calculate on a uniform basis the maximum 8-hour averaging time concentrations to be expected annually. This was done for values measured in the following situations:

1. Vehicles in downtown traffic.

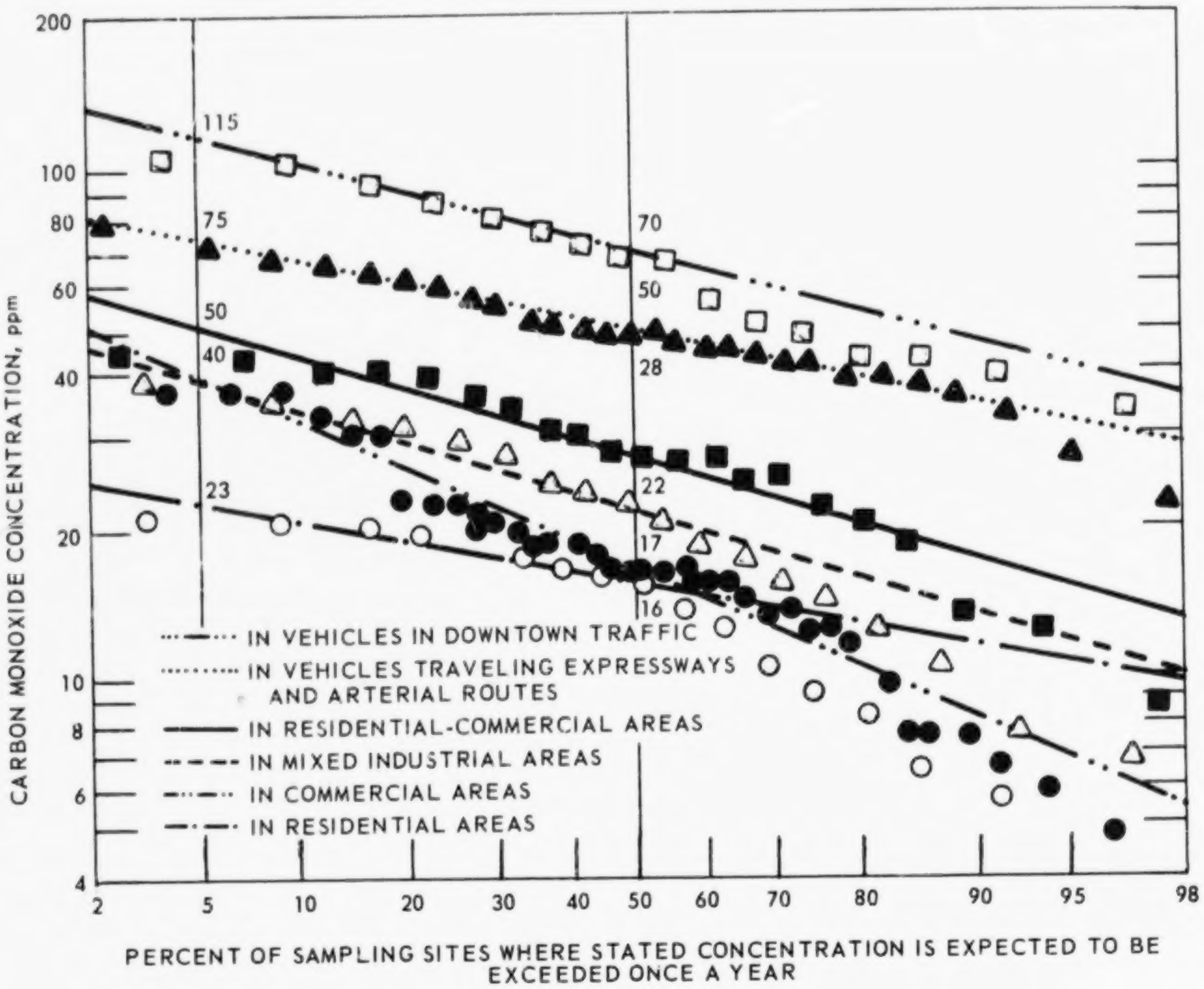

Figure 6-10. Maximum annual 8-hour-averaging-time concentrations of carbon monoxide expected at various types of sites.

2. Vehicles on expressways or arterial routes.
3. Residential-commercial areas.
4. Mixed industrial areas.
5. Commercial areas.
6. Residential areas.

The results are shown in Figure 6–10.

Studies of the first two types of exposure have been conducted.[19-34] The average citizen is not often subject to the first two types of exposure for 8 hours. Nevertheless, cab drivers, bus drivers, delivery truck drivers, and some policemen are so exposed. A number of epidemiological studies on occupationally exposed groups are discussed in Chapter 9.

Figure 6–10 shows that, if the most polluted 5 percent of the off-street central urban areas represented by the commercial classification were selected, then the maximum 8-hour annual concentration would approximate 36 mg/m^3 (40 ppm). The CO concentrations expected inside the passenger compartment of motor vehicles on city streets in heavy traffic at the most polluted 5 percent of the locations would be almost 3 times this level, or 132 mg/m^3 (115 ppm). In vehicles travelling on expressways or arterial routes, the value would be 85 mg/m^3 (75 ppm), and in residential or suburban areas the value would be about 26 mg/m^3 (23 ppm). The CO concentrations in downtown traffic appear to be about 5 times those found in residential areas. Similar findings reported by Colucci and Begeman are illustrated in Figures 6–1 and 6–2.

b. *Car Passenger Exposure to Carbon Monoxide*

Each working day a sizeable segment of the population spends considerable time driving in traffic of varying density. During that time most vehicle occupants are exposed to higher concentrations of CO than they would otherwise encounter.

The results of a study of driver exposure to CO for 20- to 30-minute periods over various driving routes are given in Table 6–5.[4,21] The results indicate that exposure levels vary with vehicular route. Average CO concentrations were highest on center city routes, somewhat lower on arterial routes, and lowest on expressway routes.

c. *Severe Carbon Monoxide Exposure Locations*

While significant concentrations of CO, which affect large subgroups of the population, occur on city streets, even higher concentrations, often exceeding 100 mg/m^3 (84 ppm), have been reported in underground garages, tunnels, and loading platforms.[25-28]

A survey was conducted recently by the National Air Pollution Control Administration at the Chicago Post Office in the Air Rights Building, which is built over a four-lane vehicle expressway. Preliminary results indicate that CO concentrations ranged from 17 to 89 mg/m^3 (15 to 77 ppm) at the east loading platform of the building, with an average concentration of 47 mg/m^3 (41 ppm). The west loading platform showed CO levels that ranged from 9 to 75 mg/m^3 (8 to 65 ppm), with an average of 28 mg/m^3 (24 ppm). Other locations and rooms showed lower CO concentrations.[29]

Chovin[28] has recorded average CO levels of 170 mg/m^3 (150 ppm) between 7:30 and 8:00 a.m. and 210 mg/m^3 (180 ppm) between 7:30 and 8:00 p.m. in the air of a Paris police garage. Trompeo[30] et al. measured the CO levels in 12 underground garages in Rome. The average CO level based on 132 readings was 113 mg/m^3 (98 ppm), ranging from a minimum of 12 mg/m^3 (10 ppm) to a maximum of 350 mg/m^3 (300 ppm). Forty-two percent of the readings showed CO levels of $\geq$ 115 mg/m^3 (100 ppm).

Waller[25] et al. reported on CO concentrations in the Blackwell and Rotherhithe Tunnels in London during periods of high traffic volume. The mean CO concentrations during the morning and evening "rush" hours were slightly more than 115 mg/m^3 (100 ppm). While the usual sampling periods were short, one of the sampling periods in the Rotherhithe Tunnel exceeded 1.75 hours. This study indicated that peak CO levels reached 600 mg/m^3 (500 ppm) at midnight on a Sunday; other peaks were 500 mg/m^3 (450 ppm) on a Friday evening and 390 mg/m^3 (340 ppm) on a Saturday evening. (The fans in these tunnels were shut off during the night, thereby reducing ventilation.) Wilkins reported earlier that CO concentrations in the Blackwell Tunnel ranged from 170 to 680 mg/m^3 (150 to 590 ppm) in September 1954. Other air samples taken in this tunnel between June and December 1955 showed CO levels ranging from 270 to 540 mg/m^3 (235 to 470 ppm) CO during the morning rush hours.[31]

d. *Indoor Levels of Carbon Monoxide*

Carbon monoxide found inside buildings may be attributable to internal sources such as space heating units and cooking stoves as well as sources outside the building.[35]

In 1969 NAPCA supported a preliminary study of the contribution of both outdoor and indoor sources to levels of CO in single-family homes.[36] Figure 6–11 shows that the major source of CO in the house with gas-burning devices was inside the house, although between 8 and 10 p.m. on Friday an outdoor source was dominant. Figure 6–12, which probably represents an extreme situation, indicates the presence of a strong CO source in the house. Further investigation showed that a leaky hand-fired coal-burning furnace was the offender.

Table 6-5. IN-TRAFFIC 20- TO 30-MINUTE CARBON MONOXIDE EXPOSURES FOR VARIOUS DRIVING ROUTES

City	Date	Center city routes					Arterial routes					Expressway routes				
			Average CO concentrations, ppm					Average CO concentrations, ppm					Average CO concentrations, ppm			
		No. runs	Min.	Avg., all runs	90th percentile	Max.	No. runs	Min.	Avg., all runs	90th percentile	Max.	No. runs	Min.	Avg., all runs	90th percentile	Max.
Atlanta	May 11–17, 1966	7	13	21	27	27	9	21	30	38	40	10	12	23	33	35
Baltimore	April 8–15, 1966	14	15	24	34	38	25	6	17	29	33	18	2	9	19	21
Chicago	May 25–June 8, 1966	17	24	32	40	55	51	7	16	21	31	31	13	24	34	37
Chicago	Feb 27–Mar 17, 1967	10	19	34	50	53	28	1	16	27	41	35	3	20	31	35
Cincinnati	Aug 2, 16, 17, 1966	8	17	29	48	50	25	3	17	26	32	7	3	10	15	15
Cincinnati	June 1967	6	12	20	32	32	11	9	15	19	19	24	7	15	24	34
Denver	Sept 19–30, 1966	10	21	34	49	54	41	11	32	47	61	24	10	21	35	38
Detroit	June 13,–July 14, 1966	16	15	25	35	36	51	14	25	33	41	48	11	25	33	54
Houston	Dec 5, 1966–Jan 29, 1967	14	16	38	60	70	23	5	15	28	33	31	2	16	33	39
Louisville	Mar 1–4, 1966	10	16	23	33	33	14	4	16	26	31	14	2	8	15	21
Los Angeles	Oct–Nov 3, 1966	17	27	40	59	60	15	24	38	58	60	87	9	29	47	62
Minneapolis-St. Paul	Aug 29–Sept 9, 1966						59	10	23	36	41	No expressway runs				
Minneapolis	Aug 29–Sept 9, 1966	15	20	30	44	45										
St. Paul	Aug 29–Sept 9, 1966	13	21	35	58	65										
New York	April 21–May 5, 1966	48	14	32	44	58	No arterial runs made					31	8	23	36	45
New York	May 1–31, 1967	30	9	27	39	42	No arterial runs made					17	5	21	38	39
Philadelphia	June 1–16, 1967	20	18	29	37	38	40	9	22	35	38	20	8	17	28	38
Phoenix	Nov 9–18, 1966	12	27	38	53	54	26	13	27	37	43	39	12	23	34	50
St. Louis	Feb 6–17, 1967	19	15	28	45	50	38	8	17	23	34	37	2	10	17	22
Washington	April 5–27, 1967	34	8	26	42	63	17	10	20	29	30	35	2	12	26	33
All	Mar 1966–June 1967	320	8	30	44[a]	70	473	1	22	33[a]	61	508	2	18	29[a]	62

[a] Estimated.

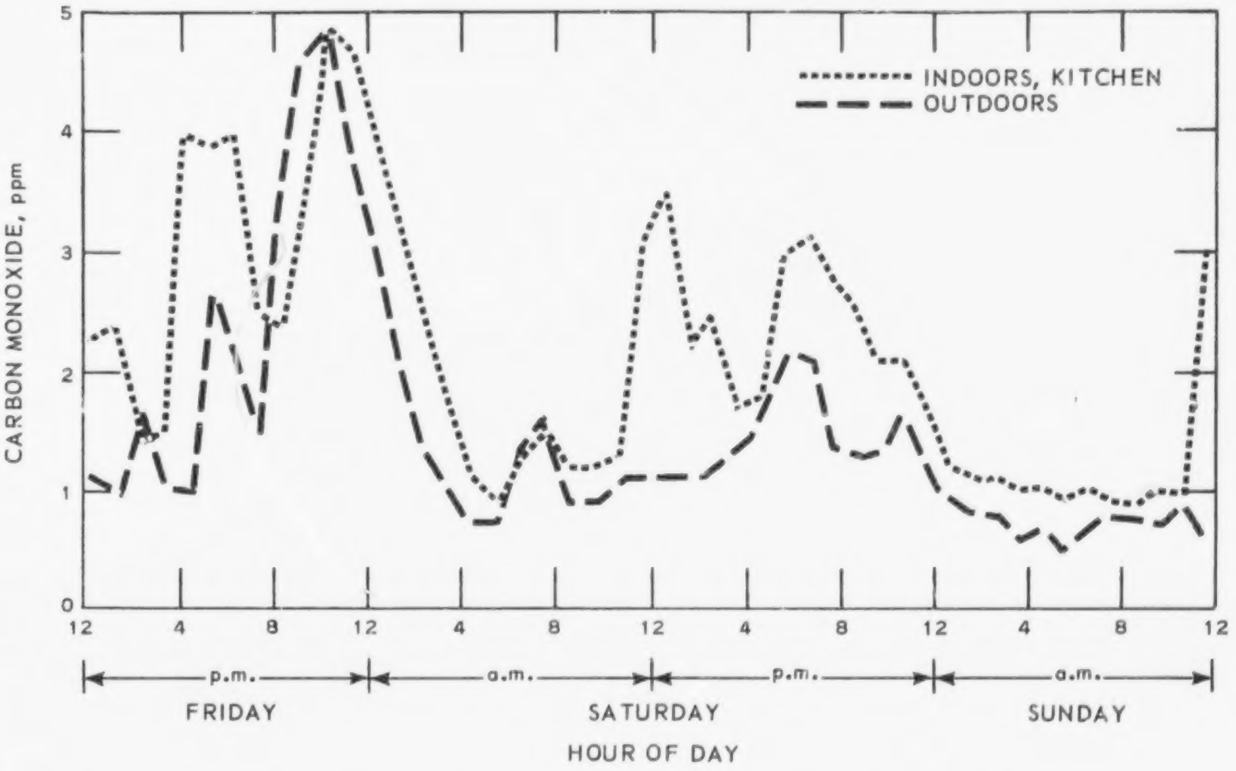

Figure 6-11. Hourly average CO levels inside and outside gas-heated house with gas-burning kitchen stove.[36]

e. Projected Future Trends

A number of studies and calculations of future CO emissions and concentrations from urban traffic data have been made; other studies are in progress. Ott[32] et al. calculated present and future CO emissions and ambient CO concentrations in Washington, D.C., using 1964 and projected 1985 traffic volumes and emission factors with a meteorological diffusion model. They found that: (1) with no emission control, the total CO emitted in Washington will approximately double in a nonuniform manner; the smallest increases will occur downtown and the greatest increases in the outskirts; (2) the principal effect of such nonuniformity, also apparent in Chicago, is to increase the area of the city exposed to high emission densities, leading to consequent increases in the area over which higher concentrations occur; (3) without control, the mean annual CO concentrations at four selected sites in Washington would range from 2.5 to 12.6 mg/m^3 (2.2 to 11.0 ppm) in 1985, representing increases of from 44 to 69 percent over the 1964 values.

A corollary to finding No. 2 above is apparent. If the area of a city subjected to high pollutant concentrations is increased, the populace in some downwind parts of that area will be exposed to high concentrations for longer periods of time than previously, because cleaner air has to come from farther away. The probability of exceeding a given 8-hour-average CO concentration is, therefore, increased; or, conversely, the 0.1 percentile level in Larsen's model[17] will be higher.

Taking the increase presented in No. 3 above to be about 50 percent implies that if maximum urban concentrations approximated 45 mg/m^3 (40 ppm) in 1965, and if CO from motor vehicles were not controlled, concentrations of about 70 mg/m^3 (60 ppm) would be expected in 1985. In-vehicle concentrations of at least twice this, or 140 mg/m^3 (120 ppm), would be expected.

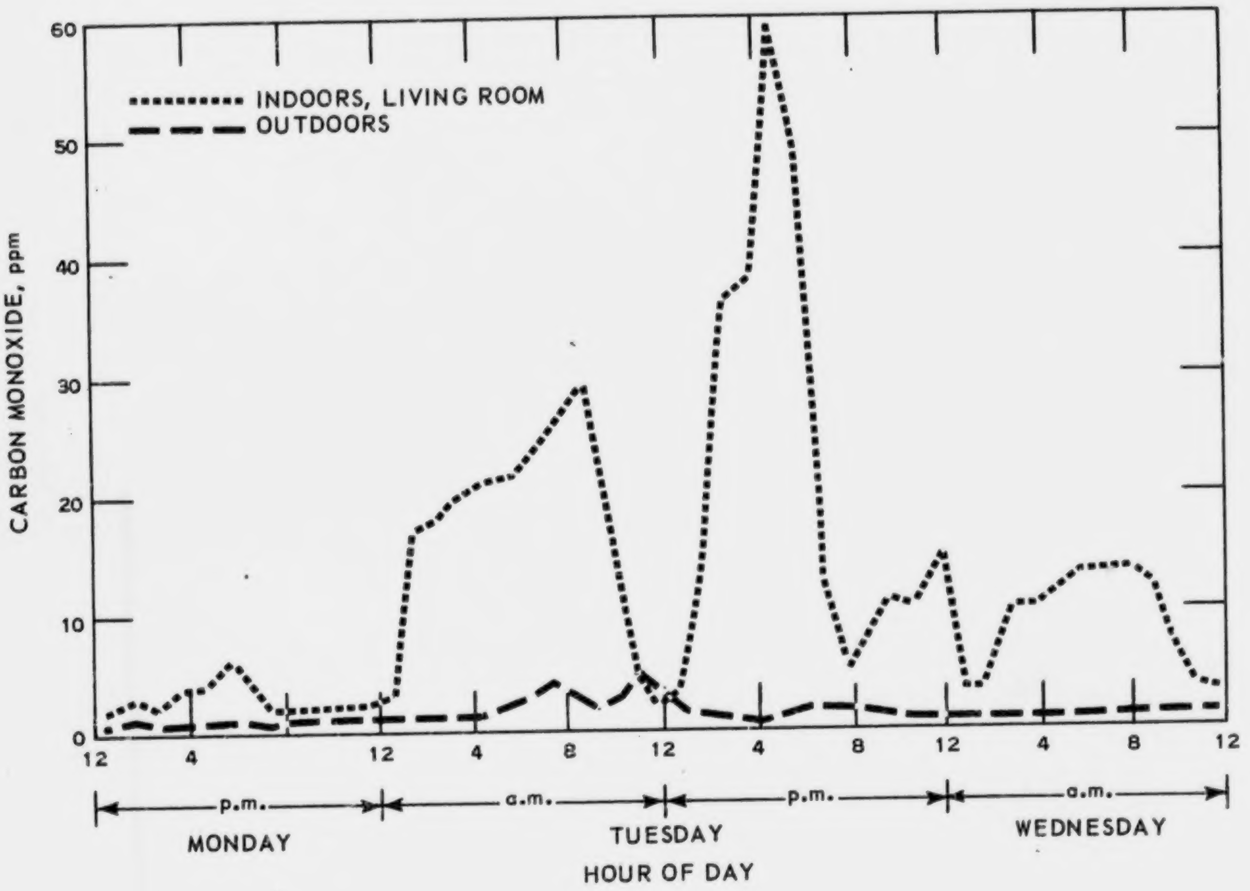

Figure 6-12. Hourly average CO levels inside and outside house heated with hand-fired coal-burning furnace.[36]

E. METEOROLOGICAL DIFFUSION MODELS

Emissions data provide a general idea of the presence of certain pollutants in a given area and may be thought of as showing the potential for exceeding an atmospheric concentration. Whether this potential is realized depends strongly on meteorological factors. These factors have, consequently, been subjected to much study. Simple meteorological indices, such as the number and persistence of low-level inversions per year, give some indication of the frequency with which unfavorable meteorological conditions occur in a particular region. In recent years much effort has gone into the development of relatively complex models that permit a quantitative estimation of the effect of weather on the dispersion of the pollutant.[32-34,37-39]

Georgii et al.[40] studied CO concentrations in Frankfurt/Main. The summarized results are:

1. The temporal pattern of CO emission in streets is determined by traffic density.
2. In cities, CO concentration distributions, both lateral and vertical, are largely dependent on wind speed and direction relative to building configuration.
3. Highest concentrations are measured during periods of rush hour traffic that occur during periods of minimal atmospheric dilution.
4. Wind flow above rooftop level is effective at street level only at speeds greater than 2 meters per second (4.5 mi/hr); at wind speeds greater than 5

meters per second (11 mi/hr) at roof height a complete mixing of the street air takes place.

5. The effect of wind direction is that higher CO concentrations are produced on the leeward sides of buildings.

The mathematical-meteorological model is a useful tool with which to examine the atmospheric impact of the various sources of CO. Although much information may be obtained from such a model, the user should be aware of the nature and limitations inherent in the particular model he has chosen for use. For example, the relative frequency of occurrence and averaging time of predicted concentrations along with limitations imposed by terrain are integral parts of every model. Such features must be evaluated before application.

The input to all diffusion models consists of emission and meteorological parameters. Normally, the former category includes pollutant emission rates and source heights, and the latter includes wind velocities and those parameters that determine atmospheric dispersion. The output from these models is usually in the form of a pollutant concentration at specified locations. The gaussian diffusion equation is the most widely accepted of its type and forms the basis of most models. Turner has described this equation and its use.[41]

The modelling of CO emission and dispersion is complicated by the fact that the chief source of CO, the motor vehicle, is a multiple source and is mobile, rather than a source at a fixed point. However, the use of CO in diffusion models also simplifies some aspects of the modelling effort. Since automotive-generated CO is usually of primary concern, source height may be considered as constant at ground level. Also, no consideration of effective residence time, i.e., removal rate of CO, is required because of the assumed stability of this pollutant in an urban environment. By incorporating into a model assumptions about the way traffic flows and distributes the CO over particular routes or throughout the city, it is possible to apply a simulation approach to this pollutant.

These models are usually used to estimate concentrations for one source-receptor pair at a time. In order to estimate the air quality at a chosen location, it is necessary to perform a large number of these individual calculations and sum the results. Additionally, the air quality of a region is determined by examining the concentrations predicted for many individual points. Because of the magnitude of the number of calculations to be performed, electronic data processing is almost always needed.

In order to evaluate the accuracy of a given model, the general practice has been to compare measured concentrations at a particular receptor location with those predicted by the model. The model usually then is "calibrated" with respect to these measured concentrations. For CO, diffusion models usually predict concentrations of 0.5 to 0.1 of those measured at the monitoring station.[32, 42-48] This difference is attributed to the effect of street traffic near the station, which is not allowed for in these models. In addition, although not nearly as important, some part of the concentrations measured in urban areas may be contributed by nonautomotive sources or by meteorological transport of pollutants from other cities. This factor also is not recognized in these models. These variables, therefore, must be accounted for in the application of such models.

In using atmospheric diffusion models, meteorologists have been called on mostly to provide estimates of seasonal or annual mean CO concentration distributions over urban areas, where spatial scales of 1 to 100 kilometers (0.6 to 62 miles) are of primary interest. For these applications, the CO emission inventories available as input to the diffusion model permit only a relatively large-scale or gross treatment of the data. The local effects connected with travel distances of less than 1 kilometer are determined predominantly by aerodynamic or micrometeorological mechanisms, rather than atmospheric diffusion and transport or macrometeorological mechanisms.

F. SUMMARY

Diurnal, weekly, and seasonal patterns of CO concentrations correspond to man's pattern of activities and to meteorological factors. Since urban CO concentrations generally correlate with the community traffic volume, there are usually two peaks in concentration corresponding to the morning and evening rush hours. Peak concentrations are higher on weekdays than on weekends and holidays because of the greater weekday rush-hour traffic volume. Distinct seasonal patterns are due primarily to both traffic and meteorological variables; the mean concentration of CO is generally higher in autumn and summer than in spring and winter.

Both macro- and micrometeorological factors affect the rate of dispersion of ambient CO. The former is a predominant factor in areawide dispersion; the latter, in local dispersion. Atmospheric stability and wind speed are important macrometeorological factors; mechanical turbulence produced by automobiles and airflow around buildings is an important micrometeorological factor.

Because of physiological considerations, the averaging time of most interest for CO is 8 hours. A statistical model has been developed to convert CO aerometric data based on various averaging times to data based on a uniform 8-hour-averaging time. Based on probability theory, the 0.1 percentile 8-hour-averaging time CO concentration approximately represents the worst 8-hour period to be expected in a year. An analysis of air monitoring data indicates that 0.1 percentile 8-hour-averaging-time urban CO concentrations vary from approximately 12 to 46 mg/m^3 (10 to 40 ppm). Analyses of CAMP data suggest that these 0.1 percentile values averaged about 3 times the corresponding median annual CO values.

A statistical analysis of CO aerometric data from 30 technical papers was made. The data were reviewed in order to calculate, on a uniform basis, the maximum 8-hour averaging time concentrations expected annually. From these calculations, it is estimated that, for the most polluted 5 percent of the urban sites, the maximum annual 8-hour average in commercial areas would approximate 46 mg/m^3 (40 ppm), in motor vehicles in downtown traffic it would approximate 132 mg/m^3 (115 ppm), and in vehicles on expressways or arterial routes the value would be about 85 mg/m^3 (75 ppm). The CO concentrations in heavy traffic in city streets were almost 3 times the CO levels found in the central urban areas, and 5 times the CO levels found in residential areas.

Concentrations exceeding 100 mg/m^3 (87 ppm) have been measured in underground garages, in tunnels, and in buildings constructed over highways.

Using emission and meteorological data, diffusion models are capable of estimating CO concentrations at a particular receptor point, thus enabling the evaluation of community air quality under a variety of conditions.

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CHAPTER 7.

EFFECTS OF CARBON MONOXIDE ON PLANTS AND CERTAIN MICROORGANISMS

A. GENERAL DISCUSSION

Plants are relatively insensitive to carbon monoxide (CO) at the lower levels of concentrations that have been found to be toxic for animals. Much of the early research on the effects of CO on plants was motivated by the assumption that the phytotoxicant in smoke and illuminating gas was CO and the knowledge that plants may be sensitive to some air pollutants at concentrations that do not affect animals. Knight and Crocker[1] were the first to demonstrate that ethylene was the effective contaminant in smoke and illuminating gases and that CO had little or no effect on plants. Much of the early literature referred to studies with impure or undetermined sources of CO. Carr,[2] who reviewed the literature up to 1961, concluded that CO was not particularly toxic to plants. Although injury from CO and ethylene was similar, 5,000 times more CO than ethylene was required to cause injury.

Most of the work on effects of CO on plants was done in the 1920's and 1930's at Boyce Thompson Institute, where Zimmerman, Hitchcock, and Crocker[3,4] exposed over 100 species to experimental concentrations ranging from 115 to 575,000 mg/m^3 (100 to 500,000 ppm). The plants were exposed to CO under bell jars or in Wardian cases, with apparently no regulation of concentration after introduction of the gas into the chamber. Exposure time ranged from 7 to 23 days. Concentrations of 115 mg/m^3 (100 ppm) caused "practically" no growth retardation, suggesting that concentrations of CO needed to affect plant growth were considerably higher than those normally encountered in ambient air.

The experiments at Boyce Thompson Institute showed that plant species varied widely in their susceptibility to CO and in symptom expression. The most important detrimental responses were: (1) epinasty (downward curl) and hyponasty (upward curl) of leaf stem; (2) increased rate of aging of leaves and stimulation of abscission of leaves, flower buds, and fruits; (3) overgrowth of lenticular tissue; (4) retardation of stem growth; (5) reduction of leaf size; (6) initiation of adventitious roots from young stem or leaf tissue; and (7) modification of the natural response to gravity, causing the roots to grow upward out of the soil.

Several researchers reported alterations of plant characteristics by exposure to CO. At a concentration of 11,500 mg/m^3 (10,000 ppm) "feminization" of plants occurred.[5,7] Female sex expression is promoted in relation to male by early formation of pistillate flowers and an increase in their numbers. The effects on flower formation, leaf epinasty, abnormal stem growth, and adventitious root formation suggest substantial elevation in auxin content in CO treated plants. Dubrovina[8] reported that seeds pretreated with CO before planting produced plants with increased leaf size. Amoore[9] described a reduction in adenosine triphosphate production during a 4-hour exposure to 460,000 mg/m^3 (400,000 ppm) of CO plus an oxygen and nitrogen mixture.

The effects of CO on microorganisms are focused primarily on inhibition of nitrogen fixation. Nitrogen fixation by microorganisms is of great importance to the life of higher-type plants. Lind and Wilson[10] showed that fixation of free nitrogen by *Azotobacter vinelandii*, a free-living nitrogen-fixing bacterium, was inhibited when cultures were exposed to 2,300 mg/m^3 (2,000 ppm) CO for 35 hours. Uptake of combined forms of nitrogen such as ammonium nitrate, ammonium phosphate, sodium nitrate, and urea were unaffected by CO levels as high as 5,750 mg/m^3 (5,000 ppm) during the same exposure time. The same authors, using the same bacteria but employing microrespiration techniques, found some inhibition of combined nitrogen uptake at 6,900 mg/m^3 (6,000 ppm) for 4 hours.[11]

Lind and Wilson[12] exposed red clover plants inoculated with *Phizobium trifolii* for 1 month to 0, 58, 115, 230, 345, 575, and 1,150 mg/m^3 (0, 50, 100, 200, 300, 500, and 1,000 ppm) of CO in separate treatments. At 0 and 58 mg/m^3 (0 and 50 ppm) CO, no inhibition of nitrogen fixation was detected, but at 115 mg/m^3 (100 ppm) a 20 percent reduction in total nitrogen production occurred. At 575 mg/m^3 (500 ppm) inhibition of nitrogen fixation was essentially complete. By comparison non-inoculated plants supplied with nitrogen in the form of ammonium nitrate showed no effects of CO at concentrations of 1,150 mg/m^3 (1,000 ppm). Parallel experiments reported in the same paper showed similar results when rate of nitrogen fixation, rather than total nitrogen, was considered.

B. SUMMARY

Carbon monoxide has not been shown to produce detrimental effects on the higher-type plant life at concentrations below 115 mg/m^3 (100 ppm) during exposures for 1 to 3 weeks. Nitrogen fixation by free-living bacteria was inhibited at exposures of 2,300 mg/m^3 (2,000 ppm) CO for 35 hours. Nitrogen fixation by efficient nitrogen-fixing bacteria in clover roots was also inhibited by 115 mg/m^3 (100 ppm) CO when exposed for 1 month.

Ambient CO levels rarely reach 115 mg/m^3 (100 ppm) even for very short periods of time. In view of this and the foregoing information concerning CO effects, a significant impact on vegetation and associated microorganisms seems improbable.

It should be pointed out that no information is available on CO concentrations in soils. Most higher plants grow with their roots in the soil, and nitrogen-fixing organisms as soil dwellers would be vulnerable to soil-borne CO. Hundreds of species of both flora and fauna, whose activities are important to soil development and to plant growth, may also be affected.

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CHAPTER 8.

TOXICOLOGICAL APPRAISAL OF CARBON MONOXIDE

A. INTRODUCTION

There is extensive documentation of the fact that high concentrations of carbon monoxide (CO) can cause many physiological and pathological changes and ultimately death. The effects of exposure to levels of CO of less than 115 mg/m^3 (100 ppm) are not so well documented. The purpose of this chapter is to evaluate the data on experimental exposure of animals and humans to CO, emphasizing both the acute and long-term effects of low CO concentrations. A recent review[1] provides additional information on most of the studies discussed in this chapter, particularly with regard to areas for future research.

The principal toxic properties of CO are based on its reactions with hemoproteins. The most important of these reactions is the reversible combination of CO with hemoglobin (Hb) to form carboxyhemoglobin (COHb). In addition to varying exposures to exogenous CO, the body is steadily exposed to a small amount of endogenous CO formed as a by-product in the course of heme catabolism; in normal humans, this amounts to about 0.4 milliliter of CO per hour. The presence of this relatively small amount of CO results in a "normal" or "background" level of COHb in the bloodstream of about 0.5 percent.

Both oxygen and CO react with hemoglobin in a very similar manner. and their transport depends on their reaction with the iron atom of the heme prosthetic group. The affinity of hemoglobin for CO is more than 200 times greater than that for oxygen.

Heme is an iron complex of protoporphyrin. The iron, in the ferrous form, combines reversibly with ligands in a ratio of 1:1. There are four heme units in the hemoglobin molecule and, hence, four molecules of oxygen or CO may be utilized in the formation of saturated oxyhemoglobin (O_2Hb) or carboxyhemoglobin (COHb). Hemoglobin may also be present in a reduced form, which is the predominant source of the darker color of venous blood. When the iron is in the oxidized form, the molecule becomes methemoglobin, which is inactive in the transport of oxygen or CO.

The dissociation curves of O_2Hb and COHb are sigmoid in shape. The sigmoid character of the dissociation curves implies that the affinity of the binding sites changes as a result of the presence of the ligand on the other sites; i.e., there are interactions between the various binding sites. These are commonly called the heme-heme interactions or allosteric effects. Since one hemoglobin molecule contains four heme units, the binding of oxygen or CO to these units may be associated with conformational changes that reflect these interactions in the protein molecule.

Carbon monoxide is potentially capable of reacting with other hemoproteins *in vivo. In vitro* it will combine with myoglobin (Mb) to from carboxymyoglobin (COMb) and may also interfere with certain enzyme systems. The biologic significance of these reactions will be discussed in Section G of this chapter.

B. THEORETICAL CONSIDERATIONS

When air containing a certain concentration of CO is inhaled for several hours, a state of equilibrium with respect to this gas is reached in which the partial pressure of CO (P_{CO}) in the pulmonary capillary blood is virtually equal to that in the alveolar and ambient air. The equilibrium of the reaction:

$$\mathrm{CO + Hb \rightleftarrows COHb}$$

depends on the partial pressure of CO and on that of oxygen (P_{O_2}) because the two gases compete for the same reactive sites on the hemoglobin molecule. The relationship is described by the Haldane equation:

$$\frac{[\mathrm{COHb}]}{[\mathrm{O_2Hb}]} = M \times \frac{P_{CO}}{P_{O_2}}$$

where [COHb] and [O_2Hb] are the concentrations of COHb and O_2Hb (usually expressed as percent saturation), and M is the relative affinity constant. At physiologic pH and temperature, the value of M is about 210, although values of up to 245 have been reported.[2] This means that the affinity of hemoglobin for CO is about 210 times that for oxygen, or that equal amounts of COHb and O_2Hb exist in equilibrium with gas mixtures containing 210 oxygen molecules for every CO molecule.

Although a number of theories and models have been proposed to explain the sigmoid shape of the oxygen dissociation curve (a plot of the partial pressure of oxygen against the percent of hemoglobin present as O_2Hb), none has adequately explained all of the various features and kinetics of the reaction of hemoglobin with ligands. At present, the Adair model[3] seems the most acceptable, although it is likely to be oversimplified since some aspects of the equilibrium and kinetics of hemoglobin cannot be accommodated within its framework. This model describes the reactions of hemoglobin in terms of four individual equilibrium and kinetic constants corresponding to the four hemes contained in the molecule. The scheme is usually written as follows:

$$\mathrm{Hb_4 + X \underset{k_1}{\overset{k'_1}{\rightleftarrows}} Hb_4X_1};\quad K_1 = \frac{k'_1}{k_1}$$

$$\mathrm{Hb_4X_1 + X \underset{k_2}{\overset{k'_2}{\rightleftarrows}} Hb_4X_2};\quad K_2 = \frac{k'_2}{k_2}$$

$$\mathrm{Hb_4X_2 + X \underset{k_3}{\overset{k'_3}{\rightleftarrows}} Hb_4X_3};\quad K_3 = \frac{k'_3}{k_3}$$

$$\mathrm{Hb_4X_3 + X \underset{k_4}{\overset{k'_4}{\rightleftarrows}} Hb_4X_4};\quad K_4 = \frac{k'_4}{k_4}$$

where Hb_4 is the hemoglobin tetramer; X is the activity of the ligand; and K, k, and k′ are the equilibrium constant, the combination velocity constant, and the dissociation velocity constant, respectively. From experimental data gathered so far, the sigmoid shape of the curve appears to be due to a very large value of K_4, which exceeded those of K_1, K_2, and K_3.[4]

Consideration of the toxicity of CO must include not only the displacement of oxygen from hemoglobin in arterial blood, but also the interference with oxygen release at the tissue level. The latter effect can be understood by a study of the O_2Hb dissociation curve as described by Roughton and Darling[5] (Figure 8-1). The presence of COHb causes a

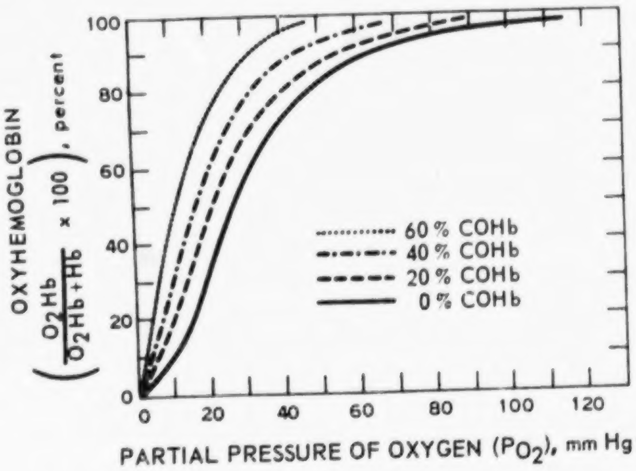

Figure 8-1. Oxyhemoglobin dissociation curves of human blood containing varying amounts of carboxyhemoglobin, calculated from observed O_2 dissociation curve of CO-free blood (pH = 7.4, T = 37 °C, P_{CO_2} 40 mm Hg).[5]

shift of the O_2Hb dissociation curve to the left for the remaining hemoglobin (not bound to CO), which implies that for a given oxygen saturation there is a lower partial pressure of oxygen. The shift of the O_2Hb dissociation curve is best understood if the most accessible binding sites are considered to be those that first pick up and discharge CO or oxygen. Essentially, the bottom part of the S-shaped hemoglobin dissociation curve is inactivated by CO; therefore only the top part reacts with oxygen. This top part, then, is reexpanded to fit between vertical and horizontal axes with altered scales for O_2Hb and P_{O_2}, respectively.

Since the increased affinity of hemoglobin for CO implies that some of the accessible sites are occupied by CO while the hemoglobin molecule circulates through the body several times, it would also mean that some of the sites that would convey labile oxygen are actually conveying nonlabile CO. The P_{O_2} of mixed venous blood (40 mm Hg) occurs at a steep part of the curve, and the effect of a shift to the left on release of oxygen at the tissue level may be considerable. This shift implies that in the presence of COHb there exists an impairment of oxygen unloading at the tissue level and thus a decreased circulatory efficiency, as estimated by oxygen delivery.

At rest, there is a close correlation between the P_{O_2} of mixed venous blood and the P_{O_2} of the tissues; hence, a lowering of the mixed venous P_{O_2} following CO inhalation reflects a similar decrease in the tissue P_{O_2}. Klausen[6] et al., using eight healthy male students as subjects, have estimated a 15 to 20 percent lowering of the tissue P_{O_2} at rest in response to the presence of an average of 15 percent COHb.

The effect of CO on the O_2Hb dissociation curve has been demonstrated experimentally *in vitro* with solutions of human hemoglobin.[3] The leftward shift of the oxygen dissociation curve has also been demonstrated by Lilienthal[7] et al. *in vivo;* the data given in their paper have been recalculated (Table 8-1) and are shown graphically in Figure 8-2. More recently, Mulhausen[8] et al. have shown that the average P_{O_2} corresponding to 50 percent O_2Hb saturation, dropped from 26.7 to 23.2 mm Hg in eight subjects who were intermittently exposed to CO and had an average of 15 percent COHb at the end of the 7-day exposure period.

In these theoretical considerations, the impairment of oxygen delivery to the tissues is only implied from the O_2Hb dissociation curve. Recently, however, Baumberger[9] et al. created an experimental model to study the oxygen delivery rate (ODR) of human blood *in vitro*. They found that the ODR increased with a decrease in percent saturation of hemoglobin and that there were significant differences in the ODR between individuals. Whether the ODR responds to small amounts of COHb at a fixed saturation of hemoglobin *in vivo* remains to be determined.

C. MEASUREMENT OF CARBOXYHEMOGLOBIN IN BLOOD

Several methods exist for the determination of blood COHb levels, but for the purpose of this document only the measurement of levels of less than 10 percent is considered. Of prime importance in this concentration range are the accuracy and reproducability of the determinations. Other aspects to be considered are the volume of blood required for accurate determinations and the sensitivity of the method to small variations in COHb. The available methods fall into three categories: nondestructive, destructive, and equilibrium methods.

1. Nondestructive Methods

The nondestructive methods are mainly spectrophotometric. Two such methods have been published recently, and both rely on the differences in the absorption between O_2Hb and COHb at given wave lengths. The advantages of these methods are: (1) a very small amount of blood is required, (2) separate determinations of hemoglobin concentrations do not have to be made, and (3) the methods are extremely simple and quick.

The first method is that of Amenta.[10] The blood samples are added to dilute solutions of ammonium hydroxide and absorbances are

Table 8–1. BLOOD AND GAS STUDIES (AVERAGES OF TWO MEASUREMENTS TAKEN 30 MINUTES APART) AFTER ADMINISTRATION OF CARBON MONOXIDE AND AIR UNTIL ATTAINMENT OF CARBOXYHEMOGLOBIN EQUILIBRIUM[7]

Subject	No. on Fig. 8–2	PaO_2, mm Hg	PaO_2 + MpCO,[a-c] mm Hg	Arterial O_2Hb, % sat.	Arterial COHb, % sat.	Arterial O_2Hb + COHb, % sat.	$100 \times \frac{O_2Hb}{COHb + O_2Hb + Hb}$	$100 \times \frac{O_2Hb + COHb}{COHb + O_2Hb + Hb}$
1 (Light smoker)	1	57.5	62.7	88.9	7.5	89.8	83.4	90.4
	2	56.0	60.9	88.1	7.3	88.9	82.9	89.7
2 (Heavy smoker)	3	40.0	48.7	80.7	15.0	83.5	72.3	85.2
	4	67.5	89.1	97.1	23.7	97.8	81.0	96.2
3 (Nonsmoker)	5	63.5	74.3	96.2	14.1	96.7	83.3	97.6
	6	54.0	59.7	89.1	8.6	90.0	82.7	90.8

[a] PaO_2 + MpCO = adjusted O_2 tension.

[b] $MpCO = P_{O_2} \times \frac{[CO]}{[O_2]}$.

[c] $M = 210 = \frac{P_{O_2} \times [COHb]}{P_{O_2} \times [O_2Hb]}$.

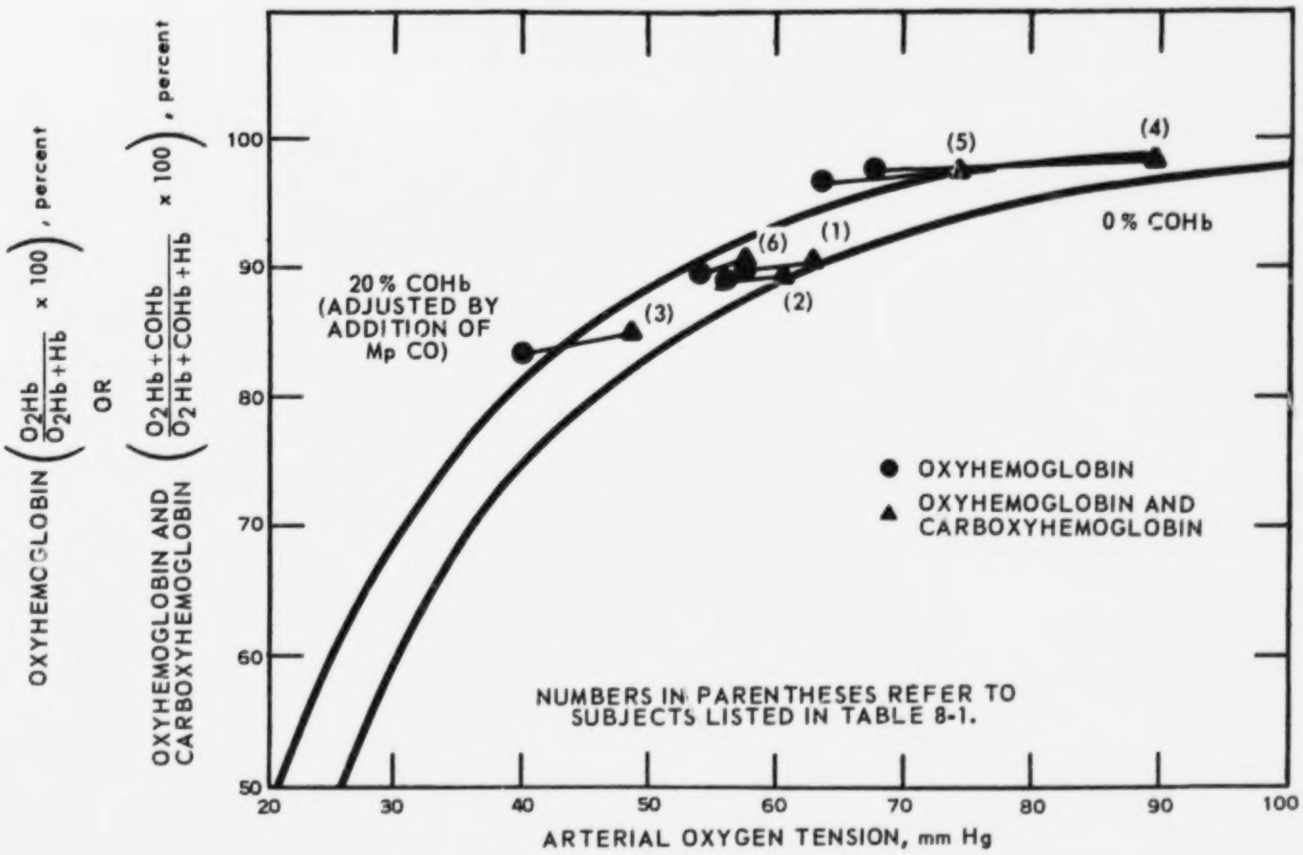

Figure 8-2. Effect of CO administration on arterial oxygen tension, compared with O_2 dissociation curves in Figure 8-1, based on data in Table 8-1.

determined at 575, 560, and 498 millimicrons (mμ). The ratio obtained,

$$R = \frac{A_{575} - A_{560}}{A_{498}} ,$$

is compared with the ratios obtained with standard solutions of O_2Hb and COHb. The percent of COHb is calculated from the equation

$$\text{Percent COHb} = 100 \times \frac{R_{O_2} - R_x}{R_{O_2} - R_{CO}}$$

where R_{O_2}, R_{CO}, and R_x are the ratios obtained, respectively, from 100 percent O_2Hb, 100 percent COHb, and the unknown COHb solution. The relationship between R_{CO} and COHb concentration is linear. Since wavelength 498 mμ is an isosbestic point, i.e., the extinction coefficients of COHb and O_2Hb are the same, the absorbance at this wavelength can also be used to determine the total hemoglobin.

Tuddenham and Hitchcock undertook to evaluate this method, but found it somewhat unsatisfactory because of the inconsistent shift induced by the varying concentrations of COHb, particularly at low levels, prevented the construction of an acceptable calibration curve.[11] The reproducibility of the isosbestic point for the determination of hemoglobin concentration, however, appeared to be satisfactory, with an accuracy to ± 0.39 percent hemoglobin.

The second method is that of Commins and Lawther.[12] In this method, the absorption of COHb is directly compared to that of 100 percent O_2Hb. The method as described in the literature is unsatisfactory for the following reasons: (1) the use of fingerprick blood is unsuitable because the varying amounts of tissue fluid contained in the different samples may lead to inaccuracies due to variations in the true volume of blood and interferences in the adsorption peaks and (2) the method of preparing standard solutions of 100 percent COHb and 100 percent O_2Hb involves bubbling CO or oxygen into the solutions. This produces an excess of dissolved gases; hence, when solutions containing less than 100 percent COHb were prepared, they were inaccurate. To overcome the above difficulties, mixed venous blood samples have been used and are equilibrated in separating funnels with either CO (as described by Amenta) or air. By mixing calculated proportions of the two solutions, an acceptable calibration curve has been prepared. From the calibration curve, it appears that the method as described is sensitive to detect a minimum of 2 percent COHb. When mixed venous blood from heavy smokers and nonsmokers was assayed for COHb, small amounts of unsaturated hemoglobin in the sample caused substantial interference between wavelengths 416 and 410 mμ. When O_2 was bubbled through the nonsmoker's blood sample, the interference disappeared, showing that the hemoglobin had become saturated. Interference caused by the saturated hemoglobin corresponded to about 10 percent COHb at 420 mμ and about 20 percent at 439 mμ. It must be concluded that the spectrophotometric methods for the determination of COHb are not suitable to measure low levels and can only be used for clinical diagnoses.

2. Destructive Methods

The destructive methods involve, for the most part, the liberation of blood gases with either total destruction of the hemoglobin or its transformation into a compound without any activity with respect to CO. The gases freed from the blood are then examined by various methods, and the CO present in them is assayed. The disadvantages of these methods are: (1) larger amounts of blood are required than for spectrophotometric methods, (2) separate determinations of hemoglobin concentrations must be made, and (3) the methods are fairly tedious. The released CO may be measured utilizing (1) detector tubes, (2) the reaction of CO with palladium chloride, (3) manometric and volumetric methods, (4) infrared spectrophotometry, and (5) gas-phase chromatography.

a. Carbon Monoxide Detector Tubes

Carbon monoxide detector tubes have been used to assay CO in gases extracted from blood. Views on the reliability of this method are varied, although it reportedly has an accuracy ranging from 2 to 20 percent when compared to the manometric method.[13] The method only gives an estimate of the CO content of blood and is not suitable for accurate determinations.

b. Reduction of Palladium Chloride by the Microdiffusion Technique

The apparatus used for this is the Conway microdiffusion apparatus. The blood gases are liberated, and the released CO reduces the palladium chloride to metallic palladium. The excess palladium chloride is usually assayed by volumetric analysis or colorimetry.[14] The method is said to be sensitive to 1 percent COHb (standard deviation of approximately ±0.03 ml/100 ml). The disadvantage is that the method is tedious and requires a skilled chemist to perform it.

c. Manometric and Volumetric Methods

Manometric methods include the techniques of Van Slyke[15] (SD ± 0.05 ml/100 ml) and Horvath and Roughton[16] (SD ± 0.03 ml/100 ml). The volumetric methods that have been successfully used are the syringe capillary method of Scholander and Roughton[17] (SD + 0.03 to - 0.05) and the Van Slyke syringe technique of Roughton and Root[18] (SD ± 0.007 ml/100 ml). These methods are accurate and considered adequate, although they are time-consuming, technically difficult, and require large volumes of blood. There is some doubt, however, as to the sensitivity of the methods at COHb levels below 5 percent.

d. *Spectrophotometric Determination of Released CO by NDIR (Nondispersive Infrared) Method*

This method calls for costly equipment, although it provides the most accurate results. Methods based on this technique have been published by Coburn[19] et al. (SD ± 0.006 ml/100 ml in the range of 0.1 to 1.0 ml/100 ml) and by Schuette.[20] Care must be taken to maintain the correct pH range and to prevent warming the blood prior to extracting the CO; otherwise, inaccurate results are obtained. A small amount of mercury is required to prevent CO formation from hemoglobin breakdown. An advantage of this method is that measurement of CO by the NDIR method is virtually specific (for a discussion on interferences, see Chapter 6, Section C.1.b on measurement of atmospheric CO by NDIR) and is considerably more sensitive than the other methods described.

e. *Gas-phase Chromatography*

Hackney et al.[21] have successfully used this method whereby the CO is released from blood in the Van Slyke apparatus, diluted, and then flushed through a gas chromatograph. The characteristics of the chromatography system are described in detail in the original paper. The sensitivity of the method is about 20 parts per million ± 1 percent with a 25-cubic-centimeter gas-sample size.

The destructive methods described provide data for only the concentration of CO in blood; to obtain the percent COHb present, separate determinations of hemoglobin must be made.

3. Equilibrium Methods - Analysis of Expired Air

This type of analysis cannot be categorized as destructive or nondestructive. Its success depends on the consideration that the lung, during breath-holding, is thought to be analogous to a closed vessel in which blood COHb equilibrates with the lung gas. Sjostrand,[22] Jones[23] et al., and more recently Ringold[24] et al. have shown that COHb may be estimated from expired air after breath-holding for 20 seconds. The subject is asked to exhale deeply, to take a deep inspiration, and hold his breath for 20 seconds; at the end of that time, the subject is asked to expire through a side arm tube. The first 150 to 250 milliliters of gas is allowed to escape, and the remaining gas expired from the lung is collected into a polyvinyl bag with a simple push-pull valve. Several studies have produced graphs correlating expired air CO with blood COHb; this is treated further in Section D of this chapter.

The method as published appears to be suitable for studying the relationship of COHb to occupational and ambient air pollution exposures where large populations need to be studied. Recent studies have shown, however, that the CO content of expired air in smokers does not always correlate well with blood COHb. Thus, further studies are required to demonstrate the validity of this method.

4. Discussion

The most accurate methods for determination of COHb are generally those that liberate and measure the CO bound to hemoglobin. The CO should be determined by the NDIR method, and the hemoglobin must be determined separately.

D. UPTAKE OF CARBON MONOXIDE BY HUMANS

References to the uptake of CO by human blood[25-35] are numerous; however, Forbes et al. in 1945 produced the first extensive study on the rate of uptake of CO by normal men.[30] Approximately 100 observations were made on seven presumedly healthy male adults exposed to from 115 to 23,000 mg/m^3 (100 to 20,000 ppm) CO for periods of up to 5 hours. Exposures to the lower concentrations were conducted in a chamber; those to the higher concentrations required the subject to inhale through a mouthpiece. Not all of the subjects were exposed to each concentration for each exposure time. Four grades of activity were used: (1) rest (subject lying upon a bed); (2) light activity (walking about chamber, taking blood samples, and reading instruments); (3) light work (riding a bicycle ergometer at 2,220 foot-pound per minute, activity equal to walking on the level); and (4) heavy work (riding a bicycle ergometer at 4,440 foot-pounds per minute, activity equal to a slow jog trot). Blood COHb was determined by the Scholander and Roughton[31] method. (Reservations pertaining to this method of analysis have been discussed in Section C of this chapter.) Although no information concerning the smoking habits of the subjects is given in Forbes' paper, the stated preexposure COHb values of 0 to 5 percent suggest that some of the subjects were probably smokers.

Nearly half of the observations were made on subjects engaging in light activity. Average results for the whole range of activities and inspired CO (0 to 23,000 mg/m^3) are given in Figure 8-3. Figure 8-3 also indicates the percent COHb increase that would be expected for the various concentrations of CO at equilibrium. Although no individual data are given in the figure, it should be noted that out of 41 observations, 18 were off the curves by only 1 percent COHb or less, 9 were off by 2 percent, 9 by 3 percent, 3 by 4 percent, and 2 by 5 percent. These individual variations are believed to be due to variation in the ratio of tidal volume to the dead space of the lung and also to the diffusion constant of the lung (DL$_{CO}$).

The data in Figure 8–3 show that the uptake of CO by the blood increases with (1) the concentration of CO, (2) the length of exposure, and (3) the ventilation rate. The rate of uptake, as estimated by the linearity of COHb with time, appears to be constant up to values of approximately one-third of the equilibrium level of COHb for a given concentration. For example, it is demonstrated in Figure 8–3 that exposure to 575 mg/m^3 (500 ppm or 0.05 percent) CO for 10, 20, 40, and 80 minutes during light work results in respective increases of COHb of approximately 4, 8, 12, and 22 percent. For this concentration of CO, the equilibrium value of COHb was calculated to be about 39 percent. These calculations are consistent with data on the rate of uptake of CO published by Pace[32] et al. and the more recent studies by Bosaeus and Friberg.[33]

In Forbes' studies, when CO was administered in 98 percent oxygen instead of in air, the rate of CO uptake decreased. This effect

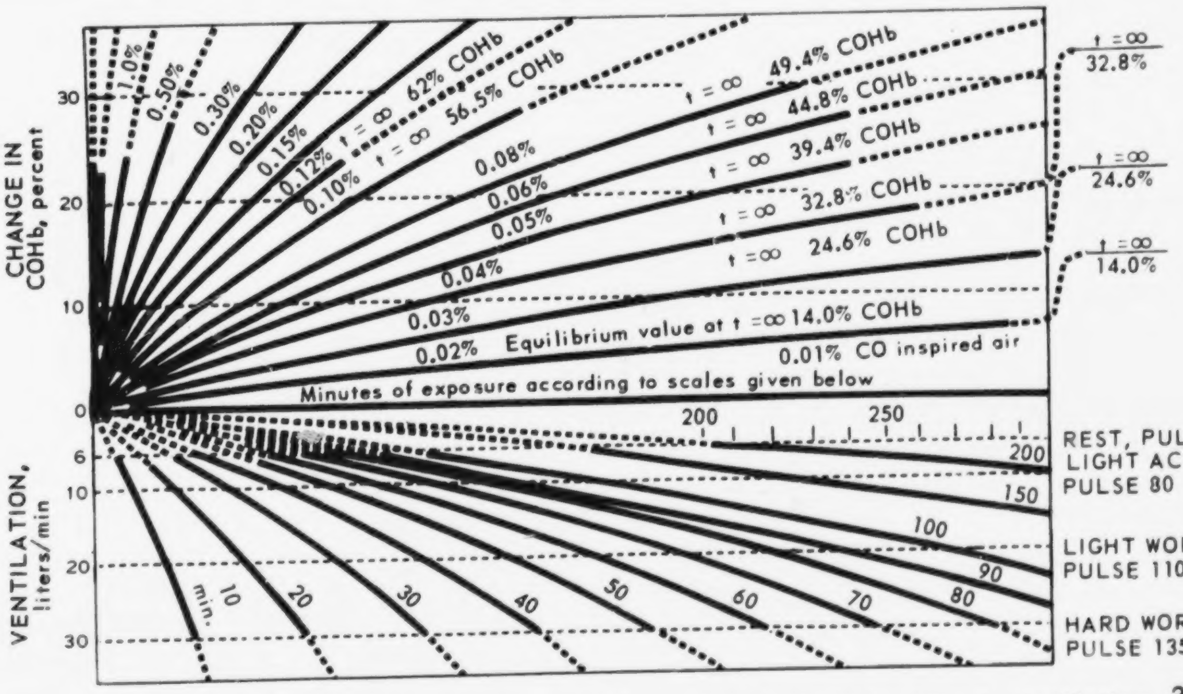

Figure 8-3. Uptake of CO at various concentrations and rates of ventilation.[30]

was more pronounced in experiments in which subjects had undergone hard work rather than remaining at rest. For reasons unknown, some subjects were found to hyperventilate in response to the 98 percent oxygen, and their apparent rate of uptake under these conditions was not the same as when the CO was in air. When a correction was made to take into account the increased ventilation, uptake at rest was reduced 23 percent and during hard work 38 percent. Exposure of four subjects to 3,450 to 4,600 mg/m^3 (3,000 to 4,000 ppm) CO for 6 minutes at an atmospheric pressure of 410 mm Hg, simulating an altitude of 16,000 feet, produced no alteration in the rate of uptake of CO when a correction was made for hyperventilation due to anoxia.[30] These experiments will be discussed more fully in Section H of this chapter.

One study made of exposure of humans to low concentrations of CO (less than 115 mg/m^3, or 100 ppm) was reported recently by Smith.[34] Ten healthy men were exposed to 35 ± 3 mg/m^3 (30 ± 3 ppm) of CO for periods of up to 24 hours. Seven of the subjects were non-smokers, and the other three were asked to refrain from smoking for at least 12 hours prior to the experiment. Blood CO was determined by the Scholander and Roughton method,[31] and hemoglobin determinations were made with a Hellige hemometer. The subjects were divided into two groups. Six subjects exposed throughout the entire 24-hour period had blood samples taken at 4, 8, 12, 16, 20, and 24 hours. Four subjects exposed for only 4 hours had blood samples taken after 0, 0.5, 1.0, 1.5, 2.0, and 4 hours of exposure. All subjects were able to rest or engage in light activity at will. The individual data are given in Table 8-2.

The average data for the nonsmokers are shown in Figure 8-4. It appears that exposure to 35 mg/m^3 of CO produces a blood level of about 5 percent COHb at equilibium. Figure 8-4 indicates that 60 percent of the equilibrium concentration was reached within the first 2 hours, 80 percent within 4 hours, and the remaining 20 percent slowly over the next 8 hours. Exposure to 35 mg/m^3 (30 ppm) of CO for 4 hours made no contribution to the blood COHb level of subject 7, a smoker. Although the preexposure COHb levels of the two remaining smokers (subjects 1 and 6) were above those of the nonsmokers, their values after 8 hours of exposure were within the same range as those of the nonsmokers.

A relatively simple formula for estimating the increase in equilibrium value of COHb above background after continuous exposure to CO concentrations of less than 115 mg/m^3

Table 8–2. **PERCENT CARBOXYHEMOGLOBIN IN BLOOD OF SUBJECTS EXPOSED TO 35 mg/m^3 (30 ppm) CO[34]**

Subject	Smoking habits	Time from beginning of exposure, hr										
		0	0.5	1.0	1.5	2.0	4.0	8.0	12.0	16.0	20.0	24.0
1	None	1.4						2.8[a]	5.6	4.2	4.7	4.7
2	None	1.0						6.0	5.0	5.0	5.0	4.5
3	Cigarettes	2.4						5.0	5.0	5.0	4.0	5.0
4	None	0.7						3.5	5.5	5.0	4.5	4.5
5	None	1.2						3.0	5.0	4.2	5.0	5.5
6	Cigarettes	3.2						3.9[a]	4.6	4.6	5.7	5.2
7	Cigarettes	5.8	5.3	5.3	5.8	4.8	4.3					
8	None	0.0	1.0	2.5	3.0	4.5	3.5					
9	None	0.9	1.3	3.8	3.4	3.4	3.0					
10	None	1.0	2.0	2.5	2.5	3.5	4.5					

[a] These samples were taken at 9.5 hr.

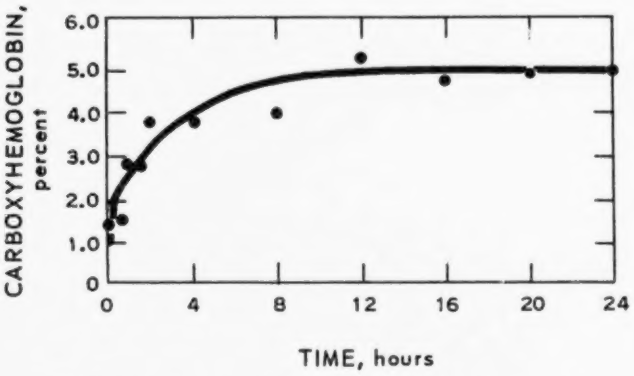

Figure 8-4. Average values of percent carboxyhemoglobin in seven nonsmokers exposed to 35 mg/m^3 (30 ppm) CO.[34]

(100 ppm) has recently been included in a review[36] of the effects of CO:

$$(\mathrm{COHb})\text{ in percent} = 0.16 \times (\mathrm{CO})\text{ in ppm}$$

Assuming a background COHb level of 0.5 percent, this formula can be expressed to estimate the equilibrium value of COHb attained after continuous exposure:

$$(\mathrm{COHb})\text{ in percent} = [0.16 \times (\mathrm{CO})\text{ in ppm}] + 0.5.$$

Thus after an exposure to 35 mg/m^3 (30 ppm) CO, the predicted equilibrium value of COHb would be 5.3 percent, which is quite close to Smith's results. Similarly, it can be anticipated from this formula that exposure to 23 mg/m^3 (20 ppm) CO for about 8 or more hours should result in a blood COHb concentration of about 3.7 percent; after exposure to 12 mg/m^3 (10 ppm) CO for about 8 or more hours, a blood COHb level of 2.1 percent would be predicted.

Experimental data are available to estimate the blood COHb levels anticipated after exposures to CO for periods of time less than would be necessary to attain equilibrium.[35] Peterson and Stewart have recently studied young human volunteers exposed to CO at concentrations s of < 1, 29, 58, 115, 575, and 1,150 mg/m^3 (< 1, 25, 50, 100, 500, and 1000 ppm) for periods of 30 minutes to 24 hours. Blood COHb was measured periodically during the experiment by both a direct determination in a CO-Oximeter and by measuring the CO liberated from the COHb using a gas chromatograph equipped with a helium ionization detector. The following relationship was derived to describe the absorption of CO by these subjects:

$$\mathrm{Log}\ \%\ \mathrm{COHb} = 0.85753\ \mathrm{Log}\ \mathrm{CO} + 0.62995\ \mathrm{Log}\ t - 2.29519$$

where CO is measured in ppm and *t* is the duration of exposure in minutes. Figure 8-5 is based on this relationship and permits the estimation of COHb levels of sedentary humans if the concentration and exposure time are known.

E. EFFECT OF CARBON MONOXIDE ON THE CENTRAL NERVOUS SYSTEM

1. Animal Data

a. Morphological Changes

Changes in the morphology of the brain and central nervous system have been observed in dogs exposed to high concentrations of CO over extended periods.

Lewey and Drabkin exposed six dogs to 115 mg/m^3 (100 ppm) CO for 5-3/4 hours a day, 6 days a week, for 11 weeks.[37] The COHb level reached each day was about 20 percent. During the exposure, no changes were observed in the electroencephalogram (EEG) or in the function of the peripheral nerves. The dogs showed a consistent disturbance of postural and position reflexes and of gait. After exposure, morphologic examinations of the nervous system showed that all animals had some indication of cortical damage. No such findings were observed in the five control animals. There were also histologic changes in the white matter of the cerebral hemospheres, the globus pallidus, and the brain stem. These changes tended to follow the course of the blood vessels. A seventh dog, which had had its posterior coronary artery ligated 1 year prior to exposure, showed the most severe cerebral changes as well as severe cardiac changes, although he was

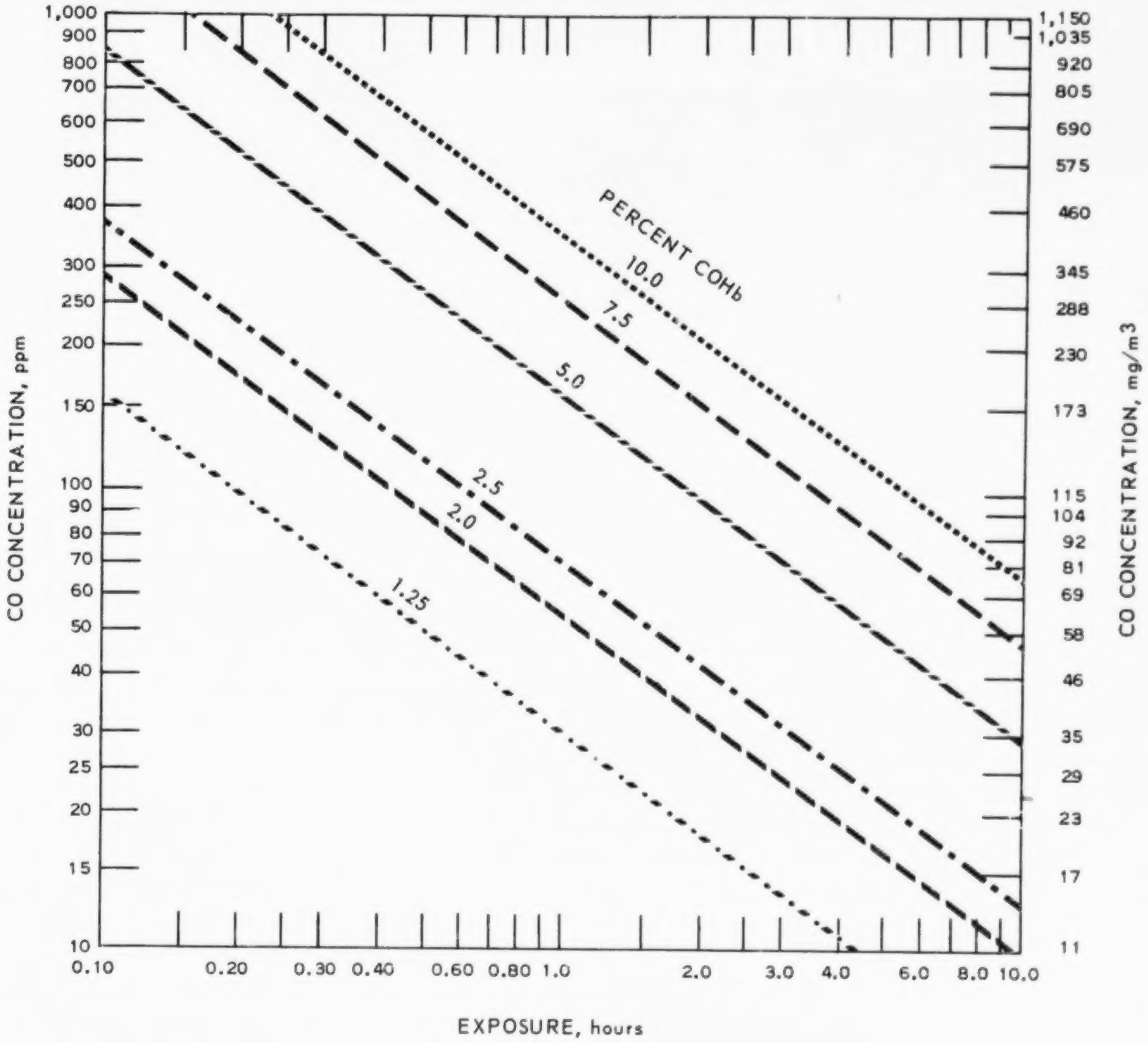

Figure 8-5. Concentration and duration of continuous CO exposure required to produce blood COHb concentrations of 1.25, 2.0, 2.5, 5.0, 7.5, and 10 percent in healthy male subjects engaging in sedentary activity.[35]

exposed for only 18 days. Although it cannot be determined whether the observed changes are attributable to acute or chronic CO exposure, these results suggest that inadequate cardiac function may predispose to cerebral anoxia and increase the risk of brain damage from CO poisoning.

In dogs that were continuously or intermittently exposed to 115 or 58 mg/m^3 (100 or 50 ppm) of CO for 6 weeks, Lindenberg et al.[38] observed that the brain showed no areas of necrosis or demyelination. There was a mobilization of glia, which suggests that a disease process was under way, and also a dilatation of the lateral ventricles. These investigators felt that brain changes were secondary to myocardial changes.

b. *Behavioral Changes*

Carbon monoxide has been found to induce behavioral changes in trained, unanesthetized, unrestrained rats.[39,40] Some studies report alterations in simple learned performance in the rat. The animal usually performs in a box that contains a lever that the rat has been taught to press. For reinforcement, the food-deprived animal receives a food pellet for some of its presses on this lever. Rats can learn to make long pauses between responses, and the ability with which the animal presses the lever has also been shown to be influenced by various drugs.

In one series of experiments conducted by Beard and Wertheim,[39] a differential reinforcement of low rate of response (DRL) schedule was used. During certain periods, the animal had to refrain from pressing the lever for more than a predetermined fixed time in order for the next lever press to be reinforced. Mean data for six rats exposed to CO are shown in Figure 8–6. Exposure to CO never exceeded 48 minutes, and all experimental sessions, including control periods, lasted approximately 2 hours. Carbon monoxide decreased the response rate on this schedule. Figure 8–6 gives the time of onset of a performance decrement large enough to fall at least 2 standard deviations below the rate measured during normal atmospheric conditions. The number to the right of each curve gives the minimum delay required of the animal for a response to be reinforced. For instance, perceptible effects were observed after exposure to 115 mg/m^3 (100 ppm) for 11 minutes when the minimum delay required was 30 seconds. It took 30 minutes of exposure to 115 mg/m^3 to produce the same relative decrement in rate when the minimum delay was only 15 seconds.

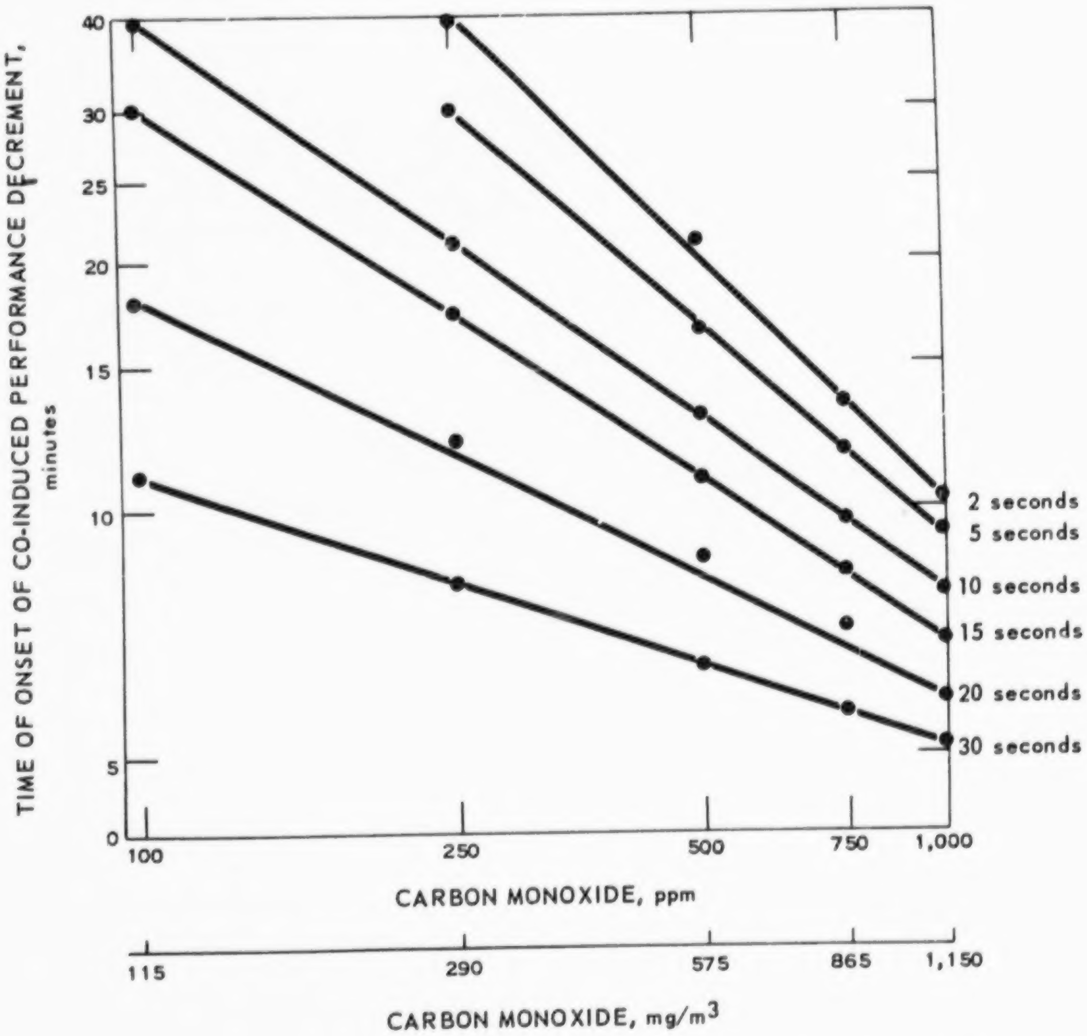

Figure 8-6. Effect of CO on mean DRL response rate in rats.[39]

Xintaras et al. have established that altered electrical activity in the cerebral cortex in rats can be observed after exposure to CO concentrations below those required to produce an impairment of performance.[40] Six adult rats were fitted with implanted electrodes, one in the visual cortex and one in the superior colliculus. The stimulus used to detect changes in these areas was a flashing light lasting 10 microseconds with a frequency of two flashes per second. A Skinner-type apparatus was used to monitor behavioral responses and was adjusted to reward each depression of the lever. When the rate of lever depression had stabilized, the flashes of light were initiated. Following an initial disruption of the lever-pressing activity, the light flash became informationally neutral and the rate of lever-pressing again stabilized. When this point was reached, the rat was considered ready for the experimental procedure. Concentrations of from 58 to 1,150 mg/m^3 (50 to 1,000 ppm) CO were used. A train of light flashes was presented to the rat while the lever was being pressed. Evoked potentials generated as a result of the flash stimuli were fed into an electronic monitoring system.

In an experiment in which the rat breathed 115 mg/m^3 (100 ppm) CO for 2 hours, no significant change in lever-pressing activity was detected when the animal was presented with a retractable lever. During this period, however, changes in the activity of the brain were recorded. These can be summarized as an increase in the amplitude of the primary component and a decrease in amplitude with an increase in latency of the secondary component. The increase in the amplitude of the first downward deflection was about 60 percent of the control value (cf. 80 percent in an experiment with 1150 mg/m^3).

At 58 mg/m^3 (50 ppm) for 1 hour, the amplitude increased by about 20 percent of control together with an increase in the latency of the second component. At 58 mg/m^3 for 2 hours, these same effects were enhanced – about a 50 percent increase in amplitude of the first downward deflection. Repeated exposures to 58 mg/m^3 for 1 to 5 hours each day for 4 days resulted in a progressive deterioration of the secondary component, as well as an associated increase in amplitude of the primary component. A post-exposure period of about 48 hours was required before these alterations in central nervous system activity returned to pre-exposure baseline level.

In an extensive series of studies on the effects of chronic low-level exposure to CO, Stupfel[41] exposed mice to 58 mg/m^3 (50 ppm) for periods of 3 months to 2 years and compared his results with appropriate controls. Animals were placed 5 days a week, 24 hours a day, into exposure chambers in groups of 3 to 10 mice. No differences between treated and control mice were found with respect to fertility, fetal survival, body growth, food intake, weight and water content of various organs, heart rate, amplitude of the QRS deflection in electrocardiographic tracings, nocturnal output of CO from the animals, and blood chemistries (including hemoglobin, glucose, proteins, lipids, cholesterol, calcium, magnesium, SGOT, and SGPT). The lethal dose of a virulent strain of bacteria was the same for exposed and control mice. Similarly, no differences were found when exposed and control mice were first vaccinated and then challenged with a larger lethal dose of the same bacteria. Mice conceived and born in exposed or control chambers were enclosed in a small air-tight chamber. At the 30th and 53rd hour of the progressive hypercarboxic hypoxia, the mortality was the same for the mice born in either chamber. Tumor growth of grafted tumors showed no differences in exposed and control animals.

The same negative results as described above were found when tests were repeated after 2 years of exposure to 58 mg/m^3 (50 ppm).

Back and Dominguez[42] performed a series of studies designed to show the effects of long-term CO exposure on performance tasks of trained monkeys. Twelve trained adult Rhesus monkeys were exposed to 55 mg/m^3 (48 ppm) CO in air for 100 days, and then to

55 mg/m^3 at a simulated altitude of 27,000 feet (5 psia in a two-gas system of 68 percent oxygen and 32 percent nitrogen) for 105 days. Successive study phases consisted of doubling the concentration of CO each 7 days following the last day of exposure to 55 mg/m^3, while maintaining the same simulated altitude. Thus, CO concentrations of 110 mg/m^3 (95 ppm), 220 mg/m^3 (190 ppm), and 440 mg/m^3 (380 ppm) were used. Performance tasks consisted of pressing levers in response to visual and auditory stimuli; avoidance of electrical shock provided the motivation to respond to the stimuli. All animals were trained on the performance tasks to a stabilized level during a period of several months prior to the CO exposure.

In the two experiments conducted at 55 mg/m^3 CO exposure, COHb saturation stabilized after the first 48 hours of exposure at 3.7 percent at sea level, and at 4.7 percent for a simulated altitude of 27,000 feet. There was no observable decrement in performance under either sea level or higher-altitude conditions. Exposure to 110, 220, and 440 mg/m^3 caused mean COHb saturations of 8.3, 19.5, and 30.1 percent, respectively. These levels produced performance decrements, in terms of reaction times and lever presses per minute, in only 2 of the 12 monkeys. Most animals performed well even under conditions where COHb attained levels of 30 percent saturation and even though changes in appetite and outward appearance occurred in 6 of the 12 animals.

These results suggest that this stimulus-response pattern of a group of well-trained monkeys was apparently not altered by levels of COHb that are clearly detrimental to humans. It does not seem reasonable, therefore, to extrapolate these results to any possible human tolerance for CO.

2. Human Data

There are several reports concerning the possibility of CO-induced impairment of higher nervous functions resulting in the impairment of human performance. One of the earliest of these experiments was conducted by Forbes[43] et al. They reported that eight normal men who were given simple performance tests simulating automobile driving were unaffected by exposure to CO until their blood COHb level reached 30 percent or more. The subjects felt normal at a COHb level of 30 percent; the two subjects who reached 45 percent COHb felt unequal to driving a car and near collapse, even though their test performance was only slightly impaired.

Schulte[44] has employed a number of psychological test procedures to determine whether any impairment can be observed at COHb levels lower than those that produce subjective symptoms. He has also sought the minimum level at which a measurable alteration in function can be detected. The following set of physiological and psychological tests was performed, and constitutes one testing cycle:

1. Pulse, respiratory rate and blood pressure.
2. Color stimulus response test.
3. Letter stimulus response test.
4. COHb determination (Scholander and Roughton method).
5. Plural noun underlining test.
6. Test of neurological reflexes.
7. Static steadiness test.
8. Arithmetic test.
9. Muscle persistence test.
10. *t*-crossing test.

Forty-nine healthy male adults aged 25 to 55 years were exposed to approximately 115 mg/m^3 (100 ppm) CO for exposure times sufficient to produce COHb levels of up to 20.4 percent. Their responses were evaluated during four consecutive testing cycles. The subjects did not know during which cycle they were being exposed to CO.

Table 8–3 shows the relationships found between the COHb levels and the tests employed. Note that there was no correlation between percent COHb and any of the physiological activities or the reaction time on the simple choice response tests (No. 1 to 8,

Table 8–3. RESULTS OF PHYSIOLOGICAL AND PSYCHOLOGICAL TESTS ON SUBJECTS EXPOSED TO 345 mg/m^3 (300 ppm) CO[44]

Test	Number of observations	Mean (range)	Correlation coefficient (between test and COHb level)
1. Pulse rate	156	72 (55-102)/min.	-0.047
2. Systolic blood pressure	156	122 (102-155) mm Hg	-0.004
3. Diastolic blood pressure	156	78 (55-90) mm Hg	-0.025
4. Respiratory rate	156	12 (9-17)/min.	-0.020
5. Muscle persistence time, left leg	156	27 (19-47)/min.	0.035
6. Muscle persistence time, right leg	156	28 (19-51)/min.	0.035
7. Letter responses	167	69.6 (49-98)/min.	0.001
8. Color responses	167	71.2 (51-99)/min.	0.078
9. Errors in letter response	167	18.0 (0-116)	0.906[a]
10. Errors in color response	167	18.7 (0-115)	0.847[a]
11. Completion time, plural-noun underlining	196	186.8 (87-317) sec	0.812[a]
12. Completion time, arithmetic	196	835 (501-1453) sec	0.665[a]
13. Completion time, *t*-crossing	196	123 (43-329) sec	0.792[a]
14. Errors in plural-noun underlining	196	17.7 (1-46)	-0.053
15. Errors in arithmetic	196	4.6 (0-12)	0.590[a]
16. Errors in *t*-crossing	196	3.4 (0-14)	0.539[a]

[a] Significant at the 0.001 level.

and 14). There was no apparent difference between the test results of the nonsmokers and those of the smokers, although Schulte considers that the number of nonsmokers in his study was too small to draw statistically significant conclusions. No data on the smoking habits of the subjects were supplied in the report, nor was there any information on the basal COHb levels of these subjects.

When the results obtained from each of the tests were further divided into 20 groups according to COHb level (0 to 0.4, 0.5 to 1.4 percent, 1.5 to 2.4 percent, etc.), it was found that the number of errors in tests 9 through 13, and 15 and 16 increased with increases in COHb level (see Figure 8–7). Schulte considers that an effect should be detectable at a COHb level of between 2 and 3 percent; however, the Scholander and Roughton method of analysis for COHb does not discriminate accurately levels below 5 percent, and hence the lower COHb measurement categories used by Schulte cannot be considered entirely accurate.

Grudzinska[45] studied the results of electroencephelograms (EEG) and other parameters of 60 workers occupationally exposed to not more than 115 mg/m^3 (100 ppm) of CO. A control group of 30 workers similarly employed but not exposed to CO was also studied. The mean level of COHb was 7 percent in the exposed group (levels of 11 subjects exceeded 10 percent) and 3 percent in the control group. Smokers from both groups had higher COHb levels than those of nonsmokers. EEG's were made at rest and after unspecified activities. A neurasthenia syndrome, which was based on subjective complaints, was diagnosed in 63 percent of the exposed group and 40 percent of the control

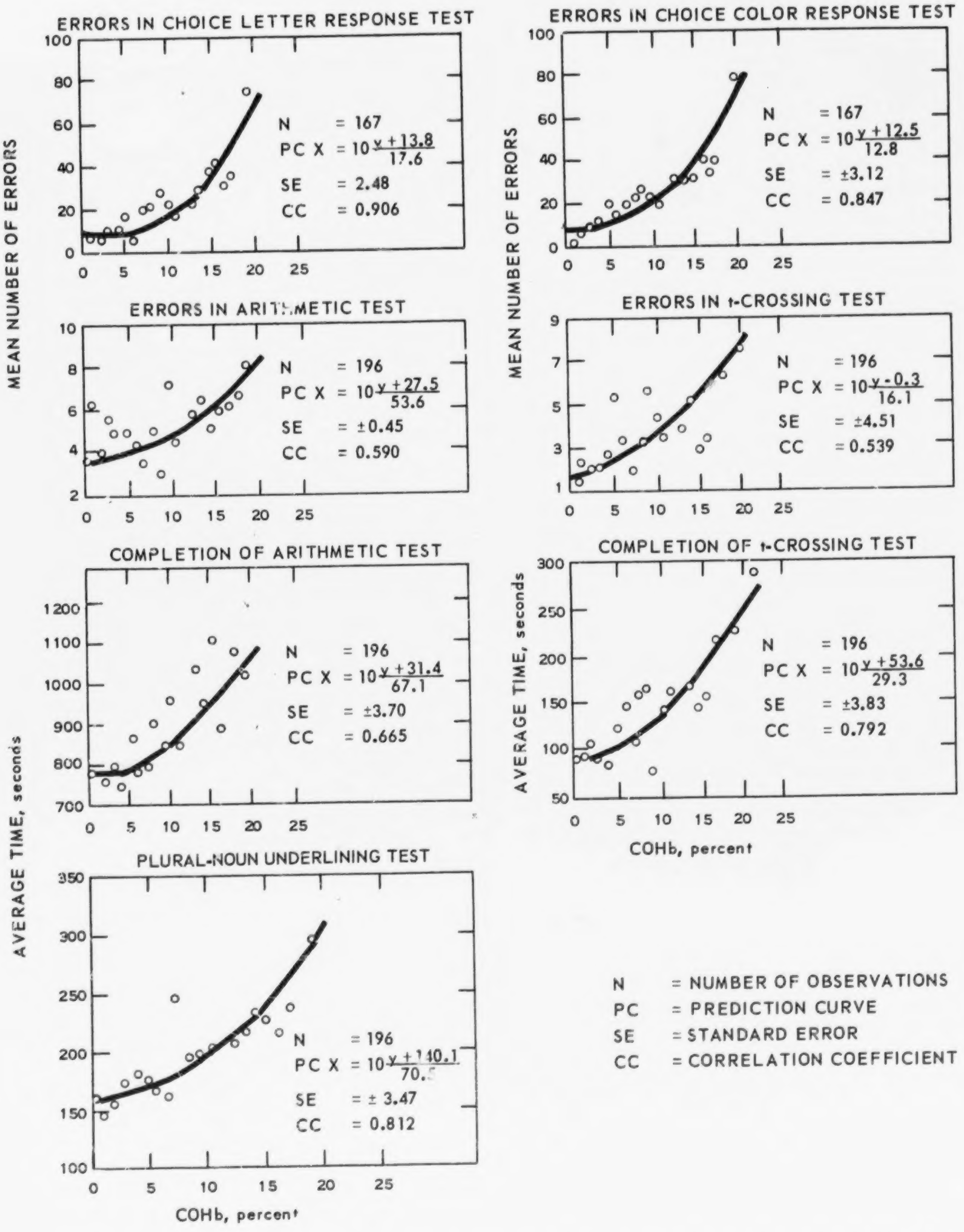

Figure 8-7. Effects of small concentrations of COHb on certain psychomotor tests.[44]

group; but there was a statistically significant increased incidence of headache and general debility in the exposed group. There was a significantly higher proportion of flat low-voltage tracings with a scanty alpha rhythm in the EEG's of the exposed group ($p < 0.01$). Since the neurasthenia syndrome had no well-defined clinical manifestations and because of the uncertainty as to whether the investigation was carried out in a double-blind fashion, these data are difficult to interpret.

Beard and Wertheim have found that CO causes an impairment of temporal discrimination.[39] Their 18 subjects were young adult university students, all of whom were nonsmokers. The subjects, seated in a soundproof booth, were presented with a 1,000-hertz tone signal, the volume of which was adjusted to well above the auditory threshold. The first or "standard" signal was of 1-second duration, and the second or "variable" signal was modulated in 18 steps between 0.675 and 1.325 seconds. The subjects were asked to indicate whether the second signal was shorter, longer, or of the same duration as the first. The comparison stimuli were presented in blocks of 25 trials; 8 were identical, 8 longer, and 9 shorter than the standard. A total of 600 trials was presented to each subject in a single session, and each subject participated in at least 15 sessions.

Figure 8–8A shows the mean percent response after exposure to 0, 58, 115, 201, and 288 mg/m^3 (0, 50, 100, 175, and 200 ppm) CO. Each point on the graph represents the mean performance at each CO dose (based upon three determinations per subject) during the second and third hours of the session, i.e., during 0.5 to 2.5 hours of CO exposure, since exposure began after the first 0.5 hour. Comparison of performance in sessions during and prior to CO exposure revealed significant impairment by "t"-test at all doses ($0.01 < p < 0.02$ at 58 mg/m^3; $0.001 < p < 0.01$ at higher concentrations). When discrimination in the differences in the duration of 125 and 325 milliseconds was considered separately,

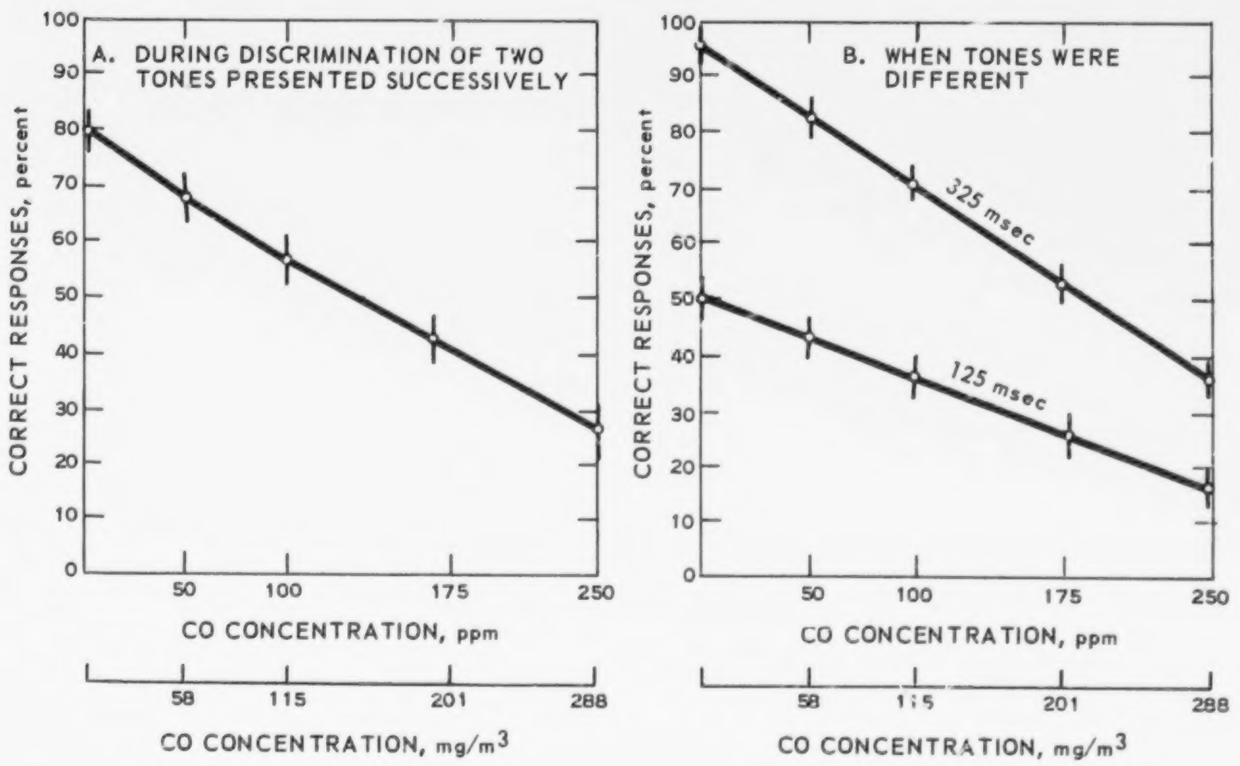

Figure 8-8. Mean percent correct responses (± one standard deviation) to 1,000-hertz tone by 18 human subjects during exposure to CO.[39]

the overall decrement for the latter was slightly greater (60 percent) than that for the former (35 percent), as is shown in Figure 8-8B. The percent of correct responses for discrimination of differences in tone duration of 325 milliseconds was 95 percent at 0 mg/m^3 of CO, compared with 50 percent when the difference was 125 milliseconds.

Data for the time taken to obtain a significant impairment of auditory discrimination are shown in Figure 8–9. A fall in the percent of correct responses was considered significant when the mean percent of correct responses fell below 2 standard deviations of the mean performance without CO. Figure 8–9 shows that only 90 minutes of exposure to 58 mg/m^3 CO may produce such a response. Unfortunately, the blood COHb levels in the studies are not available; any possible relationship between temporal impairment and COHb could not, therefore, be measured directly. From the length of exposure and the concentrations given, an increase in COHb of about 2 percent can be inferred. Assuming a background level of approximately 0.5 percent COHb, an impairment in timing behavior can be expected to occur at COHb levels of about 2.5 percent.

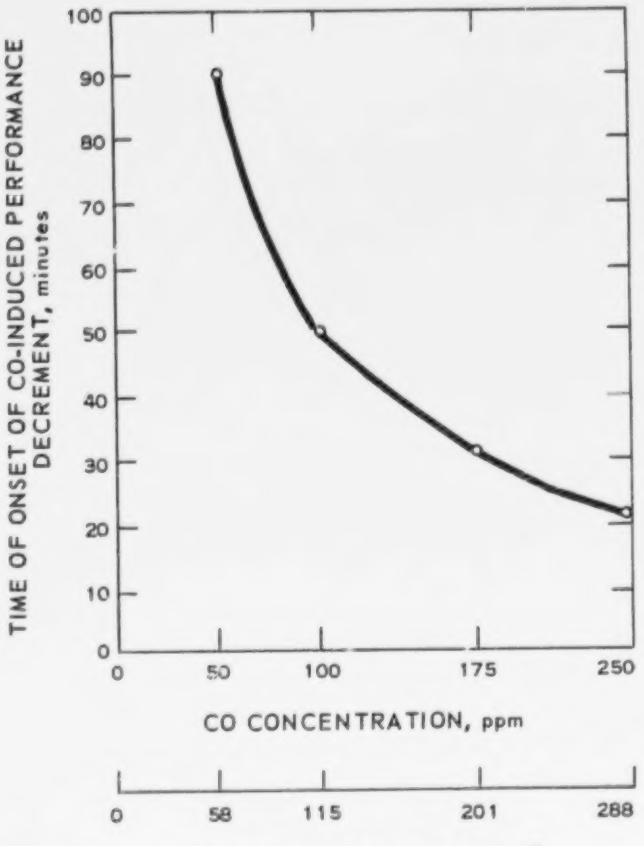

Figure 8-9. Time after initial exposure to each concentration of CO that mean correct response fell two standard deviations from mean performance level in absence of CO.[39]

Stewart[46] et al. exposed human volunteers to CO at concentrations of: less than 1, 29, 58, 115, 230, 575, and 1,150 mg/m^3 (less than 1, 25, 50, 100, 200, 500, and 1,000 ppm).

Studies were conducted in an air-conditioned exposure chamber in which CO concentrations were recorded continuously by an infrared spectrometer. Eighteen healthy males ranging in age from 24 to 42 years of age participated in the study. Only three of the subjects were smokers, and these subjects abstained from smoking for the duration of the study. Prior to and 16 hours after each exposure, blood samples were obtained for a complete blood cell count, sedimentation rate, sodium, CO_2, chloride, potassium, calcium, total serum protein, alkaline phosphatase, bilirubin, BUN, glucose, SGOT, and COHb determinations. Over the range of CO exposures from less than 1 to 115 mg/m^3, physiologic performance tests were periodically conducted during 8 hours of continuous exposure to the same CO concentration. These performance tests consisted of: hand and foot reaction time in the AAA driving simulator, Crawford screw test, hand steadiness in the AAA steadiness test, Flanagan coordination test, orthorator visual test, and time-estimation hand-reaction-time test. The latter test consisted of a series of nine tone stimuli, followed by nine light stimuli of approximately 1, 3, or 5 seconds duration presented in a random sequence. At the termination of each stimulus, the subject depressed a push-button for an interval estimated by the subject to be equal in duration to the original auditory or light stimulus. Standard EEG and visual evoked response recordings were also obtained during exposure. Following each exposure, serial venous blood samples and simultaneous alveolar breath samples were collected for COHb saturation and CO concentration.

No untoward subjective symptoms or objective signs of illness were noted during the 8 hours of exposure or in the 24-hour period following exposure. All of the clinical chemistries, including the repeat battery 16 hours after exposure, remained within normal limits. There was no detectable change from control values for any of the physiologic performance tests during an 8-hour constant CO exposure over the range of 1 to 115 mg/m^3. The latter concentration produced a blood COHb level of 11 to 13 percent.

Three subjects were exposed to 230 mg/m^3 (200 ppm) CO for 4 hours. COHb levels reached 24.8 percent within 2 hours and were associated with mild frontal headaches. All clinical chemistries remained within normal limits, but changes were observed in the visual evoked potential. The severity of headaches and changes in the visual evoked potential increased during 2 hours of exposure to CO concentrations of 575 mg/m^3 (500 ppm); this exposure produced COHb levels of 22 to 25.4 percent. During a final exposure, subjects were exposed to a constantly rising CO concentration over 2 hours until a level of 1,150 mg/m^3 (1,000 ppm) was reached. This peak concentration was maintained for an additional 30 minutes, during which the COHb level reached 31.8 percent. Although severe headaches were reported, no changes in clinical chemistries or EKG and no impairment of time-estimation ability were found. Performance on the Crawford collar-and-pin test deteriorated dramatically, and subjects reported marked fatigue of hands and fingers while performing the test. Changes in the visual evoked potential were more marked than with previous exposures.

The COHb levels were found to be so predictable and reproducible for sedentary males from one experiment to the next that they were able to be expressed mathematically as a function of exposure time and concentration. These relationships are used elsewhere in the present report.

There is some question about the sensitivity of the hand reaction-time estimation test used in the above study as a measure of performance response to CO exposure. The fact that test performance did not deviate from control even with a COHb level of 31.8 percent implies a marked degree of insensitivity, especially when noticeable fatigue of hands and fingers accompanied performance of the manual dexterity test under the same conditions. Thus, it is doubtful that these results can be used to refute the contrasting data obtained by Beard and Wertheim,[39] who employed a different performance measure for time-interval discrimination and who found consistent deterioration of performance over the range of CO exposure from 58 to 288 mg/m^3 (50 to 250 ppm). The time-interval discrimination test of Beard and Wertheim was very sensitive to CO exposure, but the different measure of time estimation employed by Stewart et al. was evidently insensitive to relatively high COHb levels.

Nine male nonsmokers, ages 19 to 22 years, were exposed to CO concentrations of 0, 58, and 144 mg/m^3 (0, 50, and 125 ppm) for 3 hours in a dome-shaped enclosed environmental system by Mikulka[47] et al. at the Wright-Patterson Air Force Base. Tests of psychomotor performance, including a time-estimation test, a tracking task, and tests of vestibular function (balance and coordination) were administered, utilizing a double-blind procedure. The exposure schedule was systematically varied to remove any effect due to training. The time-estimation test required subjects to estimate 10-second intervals on an electronic switch repeatedly for 3 minutes. Each series of tests was administered 6 times during a 3-hour exposure to each concentration of CO. Following completion of this sequence, five subjects were exposed to 230 mg/m^3 (200 ppm) and three to 288 mg/m^3 (250 ppm), and the same tests were administered. COHb levels averaged 0.96, 2.98, 6.64, 10.35, and 12.37 percent in the group of subjects after 3 hours exposure to 0, 58, 144, 230, and 288 mg/m^3 (0, 50, 125, 200, and 250 ppm), respectively. One subject reported a slight headache during exposure to 288 mg/m^3 (250 ppm), but no other subjective symptoms were reported. Group performance scores obtained during each of the 6 times the tests were administered within the 3-hour exposure period were compared with CO exposure levels of 0, 58, and 144 mg/m^3 (0, 50, and 125 ppm). CO exposures, and the associated ultimate COHb levels of 2.98 and 6.64 percent, had no effect on tests of time estimation, tracking task, or vestibular function of the group. Within each exposure level, there was also no group or consistent individual trend toward poorer performance on these tests over the course of the 3-hour exposure. The same pattern of negative results was reported for exposures to 230 and 288 mg/m^3 (200 and 250 ppm), although these results are not actually tabulated in the text of the report.

Important methodologic differences must be considered in the comparison of the results of the preceding three studies. Each group of investigators–Beard and Wertheim, Stewart et al., and Mikulka et al.–employed a different method for testing time estimation. In addition, the Stewart and Mikulka studies were conducted in a group setting where elements of competition and other stimuli to performance were present. In the Mikulka study, external distractions that might compete for the attention of the study subjects were carefully eliminated or minimized. In contrast, individual subjects in the Beard and Wertheim study were tested in an isolated booth for 4 hours; boredom or fatigue may well have added to the effect of CO to produce deviations from baseline performance when exposure and nonexposure situations were compared. The stressful element of distraction, boredom, or fatigue has been demonstrated by Mackworth to be itself detrimental to human performance of repetitive tasks.[48] The synergism between a stressful test situation, as may have been present in the Beard and Wertheim study but not in the other two studies, and CO exposure at low concentrations may account for the differences in results. Thus, differences in the method for testing time estimation and differences in conditions under which the test was administered are possible reasons for the apparently contradictory results of these three studies. The relevance of the various study results to more complex modes of behavior, particularly to automobile driving, cannot be readily judged. Although Stewart et al. and Mikulka et al. did perform tests of more complex behavior, these tests were administered in a highly artificial setting. The failure to obtain significant changes from baseline even when COHb concentrations of 12 and 33 percent were reached suggests that the undistracted attention of the subjects to the experimental setting could overwhelm the possible subtle effects of CO on performance. The same phenomenon was observed by Forbes[43] et al. in the study of the influence of CO on the ability to drive automobiles, discussed earlier in this section. Two subjects who attained COHb levels of 47 and 50 percent, respectively, were able to concentrate on their tests and perform reasonably well even though both reported that they were well aware that they were unable to drive a car; one of the subjects became unconcious for a few seconds after walking up a few steps during the test. Beard and Wertheim, on the other hand, tested a relatively simple performance task, but may have added a relevant factor, namely boredom or monotony. Apparently test method and test conditions must be considered when confirmatory studies are designed or when comparisons between studies are made. In this light, the results of these three studies are not contradictory. Until more evidence is obtained, each of the results must be considered to be highly specific to the method and conditions of testing, and extrapolations to other modes of behavior should be restricted.

Investigators other than Beard and Wertheim have reported deterioration of performance at low COHb levels. Ray and Rockwell[49] tested various automobile driving tasks performed by three young males at COHb levels of 0, 10, and 20 percent. The subjects were required to drive a car during night hours on an interstate highway while CO was administered to maintain one of the above COHb saturations. The subjects had been previously trained in the performance of each test procedure. COHb levels of either 10 or 20 percent increased the time needed to respond to taillight intensities (brakelight) and to changes in speed. These increases also altered their ability to maintain a constant speed of 65 miles per hour, to maintain a constant center-of-lane position, or to maintain a 200-foot separation from the car in front. Performance of these tasks required attention to multiple stimuli, some of which distracted the driver and prevented him from concentrating on any single task for prolonged time periods.

McFarland[50] et al. used a visual discriminometer to test effects of CO and altitude on visual thresholds of trained male subjects age 16 to 25. In this test, the subject looked through a microscope and fixed on a red point of light in an illuminated background. Measurements were made of the lowest intensity of light, presented in flashes of 0.1 second, that could be distinguished against the illuminated background. Carbon monoxide or gas mixtures containing different percentages of oxygen to simulate various altitudes were administered through a closely fitting mask during the test procedure. The concentration of COHb in finger-prick blood at the beginning of the experiment and 10 to 15 minutes after each CO administration was determined by the microgasometric method of Scholander and Roughton. COHb level during CO administration ranged from 5 to 20 percent. As shown in Figure 8–10, the visual threshold increased (i.e., the light had to be more intense to be distinguished against the background) as COHb levels increased over the entire range of exposure. The effects of CO hypoxia and simulated altitude were practically equivalent in this test. That is, the effect of a given COHb level was the same as that of an equal loss of percent O_2Hb from high altitude. These results clearly showed changes in visual threshold at COHb levels as low as 5 percent; the same magnitude of change in visual threshold was produced by a simulated altitude of approximately 8,000 feet.

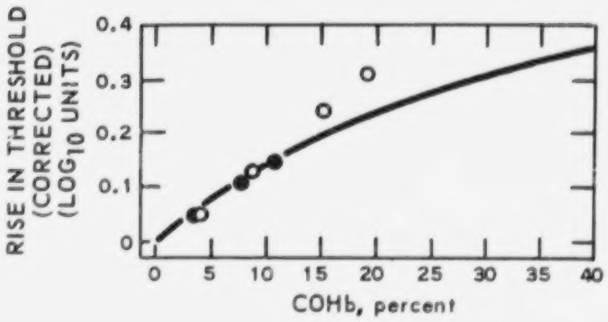

Figure 8-10. Relation between COHb and visual threshold.[50]

Beard and Grandstaff[51] recently reported the results of CO exposure on a second test of timing function. While individually isolated in a noise-insulated exposure chamber, seven subjects estimated the passage of 10- and 30-second intervals. Estimation of 10-second intervals was not affected by CO exposure. A highly significant dose-related performance decrement occurred, however, with attempts to estimate 30-second intervals. Exposures of 64 minutes at 58 mg/m^3 (50 ppm) produced significant impairment. In the same report, studies of Wertheim on the effects of CO exposure upon visual performance were reported. Four tests of visual function at various levels of brightness were conducted. Four subjects were exposed in random order to CO concentrations of 0, 58, 173, and 288 mg/m^3 (0, 50, 150, and 250 ppm), for a total exposure time of 1 hour on each test day. Exposures were always preceded and followed by performance testing without CO. Subjects were individually isolated in exposure booths for a period of 2-1/2 hours on each study day. Results of these studies, shown in Table 8–4, indicate consistent impairment of visual performance for three of the four measures of visual function. COHb levels were estimated from expired air samples. At each CO concentration, there was a rapid recovery in performance subsequent to the exposure; test results returned to normal more quickly than did the CO concentrations in the expired air.

Table 8–4. EFFECTS OF VARYING CO EXPOSURE ON VISUAL PERFORMANCE[51]

	CO exposures producing significant impairment			Estimated COHb level, %	Degree of impairment, %
Test of visual performance	Concentration, mg/m^3	Concentration, ppm	Time, min.		
Relative brightness threshold	58	50	49	3.0	4.4
	173	150	17	3.0	5.0
	173	150	49	5.0	8.0
	288	250	17	4.0	3.6
	288	250	49	7.0	8.6
Critical flicker fusion frequency	58	50	50	3.0	5.0
	173	150	50	5.0	8.0
	288	250	50	7.5	2.0
Visual acuity	58	50	27	3.0	5.5
	58	50	60	3.3	17.5
Absolute threshold for light	0 to 290	0 to 250	17 to 60	---	No consistent effect

Halperin[52] et al. exposed four healthy male adults aged 16 to 25 years to measured amounts of pure CO ranging from 100 to 300 milliliters. The CO was injected slowly into the intake tube of a close-fitting mask. The usual duration of the experiment was from 3 to 4 hours. The total length of exposure to CO was from 10 to 15 minutes, and this resulted in COHb levels of up to almost 20 percent. Visual threshold determinations were made at 10-minute intervals throughout the experiments. The subjects sat in a darkened room and looked with one eye into a microscope. Each subject saw a large circular field, uniformly illuminated at an intensity of about 0.002 foot-candle. The center of the field contained a small point of red light to serve as a fixation point. Just below the latter, a 1 x 1 degree object was presented in flashes of 0.1 second. The lowest intensity distinguishable against the dim background was determined from the mean of 10 measurements in each test. As can be seen in Figure 8–11, a measurable impairment in visual function was detectable when the blood COHb concentrations reached 4 to 5 percent; at higher COHb concentrations, greater degrees of impairment were measured. Control experiments, in which innocuous odors were introduced into the intake tube of the facial mask, showed no significant change in visual discrimination.

In the same series of experiments, a study of hypoxic anoxia was made in which normal air was replaced by nitrogen-oxygen mixtures. The oxygen concentrations ranged from 16 to 9 percent, thus producing simulated altitudes ranging from 7,000 to 20,000 feet. During recovery from the CO exposure or the anoxia, the subjects breathed either room air, 100 percent oxygen, or "carbogen" (consisting of 93 percent oxygen and 7 percent carbon dioxide). No visual determinations were made on the subjects while they breathed "carbogen," since the latter induced respiratory movements which interfered with foveal fixation and thus influenced the visual tests. The subjects were not told which gas mixture they were breathing. (However, it can be assumed that "carbogen" produced some hyperventilation of which the subjects were aware.) The blood COHb was determined by the gasometric method of Scholander and Roughton.[30] Measurements were taken at the beginning of the experiment, at 10 to 15 minutes after each CO administration, and at 20- to 30-minute intervals during the post-exposure period. The results of a typical experiment are shown in Figure 8–11.

One of the most important findings was that recovery from the detrimental effects of CO on visual function lags behind the elimination of CO from the blood; this impairment

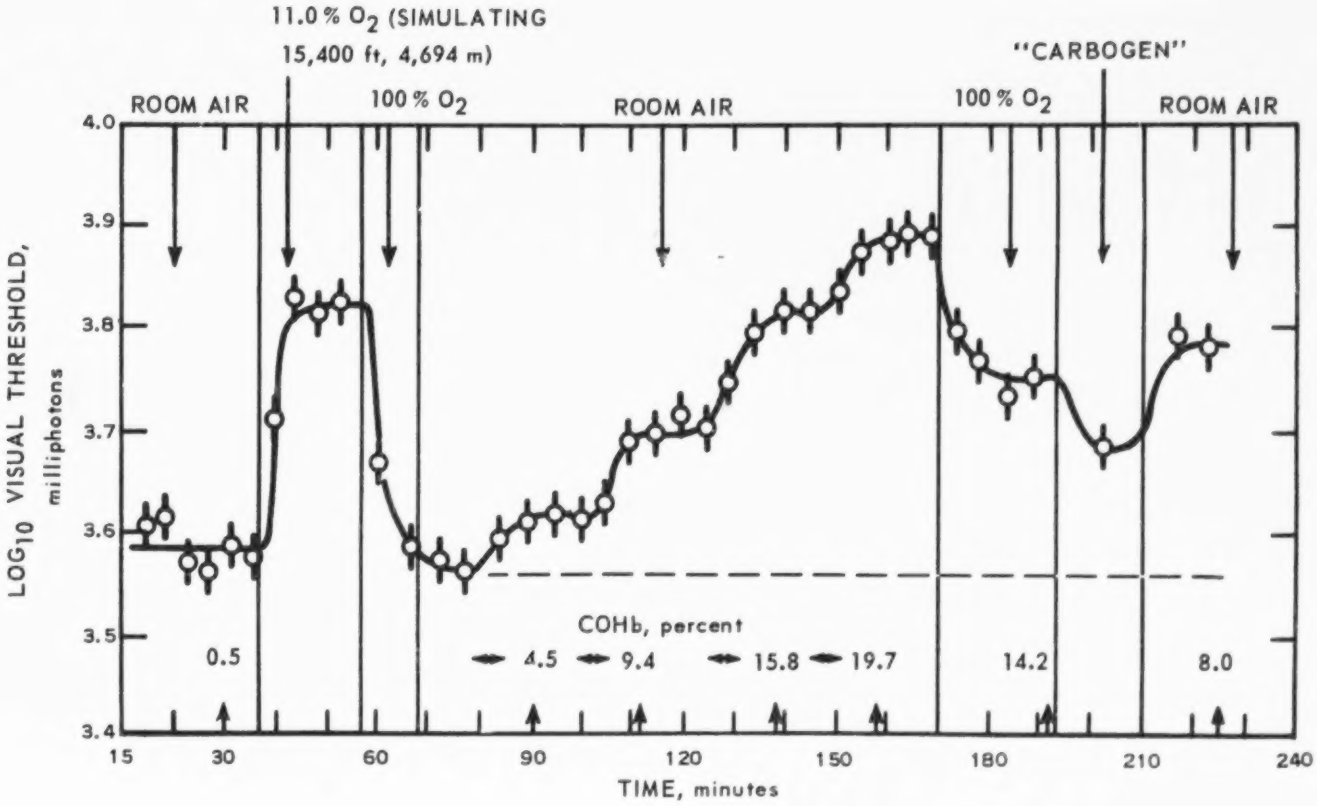

Figure 8-11. Effect of progressive increases of blood COHb on visual threshold, and of oxygen and carbogen (93% O_2 + 7% CO_2) in counteracting this effect.[52] (↔ Indicates time during which CO exposure occurred; ↑ indicates point at which blood was taken for COHb determination).

appears to be determined by the duration of the presence of CO as well as by its concentration. The time course followed by the COHb and visual impairment appears to depend on the composition of the gas during the post-anoxic period. "Carbogen" was 2-1/2 times more effective than 100 percent oxygen in promoting CO elimination and an associated drop in the visual threshold. Subsequent exposure to room air caused an increase in the visual threshold (i.e., further impairment in visual perception), although the COHb levels began to fall (Figure 8–11). When a single subject was exposed to CO at simulated altitudes, his pattern of results was similar to that at sea level. The latter series of experiments is discussed more fully in Section H.

The results reported in Halperin's paper are selected from individual subjects. No data are given to indicate the degree of variation among subjects, or the degree of variation for an individual from day to day. There is no indication as to whether an individual's threshold level when breathing unpolluted room air remains the same over a period of 3 to 4 hours. In addition, no statistical level of significance was applied to the elevation of the visual threshold above the basal level, though standard deviations are shown for the graphed data. Data on smoking habits of these subjects was not given in the report; however, in a preliminary series of experiments on one of the same subjects, it was observed that inhalation of the smoke of one cigarette produced a blood level of 2 percent COHb and caused a distinct impairment of visual sensitivity. After three cigarettes the blood COHb was 4 percent, and the effect on visual sensitivity was equal to that produced by hypoxic anoxia simulating an altitude of almost 8,000 feet.[50]

In a study by Hanks[53] performed at the Rancho Los Amigos Hospital environmental control chamber, groups of five nonsmoking healthy young males were exposed in random order to CO continuously for 4 hours. CO concentrations ranged from 0 to 115 mg/m^3 (100 ppm). A critical tracking task and visual pursuit tasks were unaffected by the exposure to CO. Test subjects were untrained in performance of these tasks, and both learning effects and effects of competition within groups were reported.

3. Discussion

Several reports on psychomotor effects of CO exposure appear to be in conflict, but explanations have been presented to account for the apparent inconsistencies. It is quite likely that some of the performance impairment associated with CO exposure can be overcome by attention to the task assigned. The major tasks of importance with which CO might interfere, e.g., those involved in driving on a highway or a street, could very well arise unexpectedly and not be subject to extra attention by the exposed individual. Perhaps what one really should be testing, then, is vigilance.

The sensitivity of the results obtained by Beard and Wertheim,[39] Ray and Rockwell,[49] and McFarland[50] are in marked contrast to many other studies. Again it should be emphasized that their results should be considered highly specific to the methods and conditions of testing. It is likely that external stimuli may have to be examined along with CO exposure to detect the subtle effects of the latter. Subsequent studies should, therefore, account for the effects of extraneous factors such as sounds, fatigue, boredom, and other distractions, and should further evaluate the possibility of an interaction between such stimuli and the task performance thought to be affected by exposure to CO.

Since it is amply demonstrated that subjects smoking cigarettes are likely to have measurable and possibly significant increases in COHb levels, it is important to carry out studies either on nonsmokers or on individuals whose smoking exposures are clearly defined and whose baseline COHb levels are established. At the present time, it is uncertain to just what extent smokers do adapt to prolonged increases in blood COHb levels.

F. EFFECTS OF CARBON MONOXIDE ON CARDIOVASCULAR SYSTEM

1. Animal Data

a. Short-Term Exposure

Lindenberg[38] exposed 27 dogs to concentrations of CO greater than 1,150 mg/m^3 (1,000 ppm) for 1 to 4 hours. A second group of 11 dogs was exposed to an air-nitrogen mixture producing an oxygen deficit equivalent to that caused by CO inhalation. In animals exposed to CO, the COHb levels reached 37 to 40 percent. In all animals where EKG's were recorded (13 out of 27), a depression of the R-wave, elevation of the ST segment, an occasional increase in the T-wave, and deepening of the Q- and S-waves were recorded. In some animals, these changes in EKG and associated irregularities of the heart action (premature ventricular contractions resulting in the abolition of arterial pulsation) persisted for several days. In the dogs subjected to severe hypoxia, the EKG changes were essentially the same as those seen in dogs exposed to CO. At autopsy, the hearts of several animals revealed dilatation of the ventricles, especially the right one. In four CO-exposed and two hypoxic animals, small areas of muscle necrosis were observed, as well as fine granular fatty degeneration of muscle fibers in certain areas, particularly in the interventricular septum and in the outer wall of the right ventricle.

b. Long-Term Exposure

Two studies have revealed that continuous exposure of animals to low levels of CO can cause cardiac changes. Ehrich[54] et al. exposed four dogs to about 115 mg/m^3 (100 ppm) CO for 5-3/4 hours a day, 6 days a week for 11 weeks. The resulting average COHb level was

21 percent. A second group of six dogs was exposed to air in which the oxygen content was reduced to 10 percent. The authors considered that this led to a P_{O_2} in the blood approximating that which would be present at a blood level of 21 percent COHb. These exposures were continued for 4-1/2 hours a day, 6 days a week for 11 weeks. All animals were sacrificed 3 months after the termination of the experiment. No EKG changes were observed during the first week. After the second week, however, one CO-poisoned dog and one hypoxic dog exhibited inversion of normally upright T-waves. Another hypoxic dog developed an elevation of the ST segment. A second CO-poisoned dog developed an inverted cone-shaped T-wave during the tenth week. These EKG changes appeared to be irreversible, since they continued unabated until about 3 months after the exposures when the animals were sacrificed. The authors noted the resemblance of these EKG changes to those typically seen in myocardial anoxia. The gross appearance of the hearts was normal, but microscopic examination revealed that all four CO-poisoned animals and one oxygen-deficient animal had marked degenerative changes in individual muscle fibers. It should be noted that one control dog showed similar changes, although the number of control dogs used in this study was not reported.

Lindenberg[38] exposed 15 dogs to 58 mg/m^3 (50 ppm) CO for 6 weeks. Seven of the dogs were exposed for 6 hours a day for 5 days a week. Eight were exposed continuously for 24 hours a day, 7 days a week. A second group of eight dogs was exposed to 115 mg/m^3 (100 ppm) CO on a similar schedule, four intermittently and four continuously. Five dogs were used as controls. All dogs were sacrificed a few days after the end of the experiment. The dogs exposed to 58 mg/m^3 developed blood COHb levels of from 2.6 to 5.5 percent. There were no changes in the hemoglobin content or hematocrit. Five intermittently and five continuously exposed dogs developed EKG changes during the third week similar to, but less severe than, those observed from short-term exposures to higher concentrations. Higher COHb levels in dogs after exposure to 58 mg/m^3 (50 ppm) CO were reported by Musselman[55] et al. in another study (see below).

The dogs exposed to 115 mg/m^3 developed COHb levels of from 7 to 12 percent. Somewhat higher COHb levels would have been expected in man after similar exposures.[38] All dogs showed abnormal EKG recordings after about 2 weeks, with depression of the R-wave voltage, elevation of the ST segment, occasional deepening of the Q-wave, and occasional premature ventricular contractions. At autopsy, the most frequent finding was a dilatation of the right heart chambers, and also, occasionally, of those on the left side of the heart. Histologically, some hearts showed degeneration of muscle.

In contrast, Musselman[55] et al. exposed 100 rats, 40 rabbits, and 4 dogs to 58 mg/m^3 (50 ppm) CO for 24 hours a day, 7 days a week for 3 months. No changes were noted in the EKG's or the pulse rates of the dogs. Moreover, pathologic examination of organs and tissues revealed no differences between exposed and control animals in any of the three species. The average COHb levels reached were 7.3 percent for dogs, 3.2 percent for rabbits, and 1.8 percent for rats. The dogs showed significant increases in hemoglobin levels (12 percent), hematocrit (10 percent), and red blood cell (RBC) counts (10 percent). It should be noted that the increase in the RBC count in one dog alone accounted for over half the total increase established by the whole group (Table 8–5).

Roussel[56] et al. have detected reversible EKG changes in rodents exposed to CO. Rats were exposed to 17 and 58 mg/m^3 (15 and 50 ppm) CO for 24 hours a day for 3 months. The exposures to 58 mg/m^3 caused a slight decrease in the QRS voltage during the first 2 weeks of exposure; this subsequently returned to normal despite continued exposure. No changes in heart weights were observed. Although there were increases in hemoglobin level, hematocrit, and RBC counts, they were significant only at the $p = 0.10$ and $p = 0.15$ levels.

Table 8–5. PERCENT CHANGE IN BLOOD VALUES OF INDIVIDUAL DOGS IN RESPONSE TO 58 mg/m^3 (50 ppm) CO INHALATION DAILY FOR 3 MONTHS[55]

Dogs	Dog ID number[a]	Hemoglobin	Hematocrit	RBC count
Unexposed	191	-2	-6	-2
	192	-2	-5	-5
Mean		-2	-5.5	-3.5
Exposed	124	+7	+5	+6
	185	+10	+8	+4
	188	+14	+14	+8
	193	+16	+11	+22
Mean		+11.75	+9.5	+10.0
Statistical significance of change		$p < 0.05$	$p < 0.10$	

[a] Each line of data is from a single animal.

Astrup[57] et al. have recently reported that cholesterol-fed rabbits continuously exposed to CO for 10 weeks (with exposure levels sufficient to produce COHb levels of 15 percent for 8 weeks and 30 percent in the last 2 weeks) developed cholesterol deposits in aortic tissue at a rate 2.5 times faster than nonexposed cholesterol-fed animals. Intermittent CO exposures for 8 hours a day for 10 weeks (sufficient to produce COHb levels of 20 percent) resulted in a fivefold excess in the cholesterol content of aortic tissue of exposed versus control rabbits. Cholesterol feeding and hypoxia (10 percent oxygen in nitrogen) produced similar effects, but to a lesser degree. Carbon monoxide exposure without cholesterol feeding induced arterial lesions consisting of endothelial hypertrophy and proliferation and focal subintimal edema: these lesions could not be distinguished from those associated with spontaneous arteriosclerosis occurring in rabbits. The authors speculated that CO or hypoxia enhanced the development of atheromatosis by increasing vascular permeability to lipoproteins.

The effects of acute high-level and chronic low-level exposure to CO on cardiovascular and cerebral function and morphology in dogs has been studied by Preziosi.[58] Acute exposure to CO concentrations exceeding 1,150 mg/m^3 (1,000 ppm) and producing maximum COHb levels of 3 to 40 percent, resulted in high mortality and, in survivors, sudden rises in cerebrospinal fluid (CSF) pressure and EKG changes (consisting of depression of R-waves, elevation of the ST segments, and deeping of the Q-waves). Major voltage depression and complete abolition of electrical potentials of the EEG occurred only after the EKG showed severe changes. No gross pathology was observed in the brains of surviving dogs, but histologic alterations were noted, ranging from microglial reactions to extensive necrosis of the white matter. In the heart, small areas of muscle necrosis and fine granular fatty degeneration of muscle fibers were found. Chronic intermittent and continuous exposure of 15 animals to 58 mg/m^3 (50 ppm) CO and of 8 animals to 115 mg/m^3 (100 ppm) CO for 6 weeks resulted in EKG changes similar to, but of lesser magnitude than, the changes in the acute exposure studies in the majority of dogs. COHb concentrations reached 2.6 and 5.5 percent in dogs intermittently or continuously exposed to 58 mg/m^3 (50 ppm), respectively, and 7 and 12 percent in the 115 mg/m^3 (100 ppm) exposure group, respectively. At autopsy, the most frequent finding was a dilatation of the right cardiac chamber and dilatation of the lateral ventricles of the brain.

2. Human Data

a. *Studies of Oxygen Debt*

As a result of observations that the oxygen debt* accumulation in response to exercise is significantly greater in smokers than in nonsmokers,[59, 60] Chevalier[61] et al. have attempted to determine the cause of the difference. In their study, CO was inhaled by ten nonsmokers to raise blood COHb levels to the range seen in a control group of nine smokers. Pulmonary function measurements were made before and after a 2.5- to 3.5-minute period, during which gas containing 5,750 mg/m^3 (5,000 ppm) CO in compressed air was inhaled. A standard excercise test consisting of a 5-minute exercise period on a bicycle ergometer was employed; the work load was the same for each subject. Measurements of oxygen uptake were obtained at 30-second intervals during a 4-minute period of rest, a 5-minute period of exercise, and another 10-minute period of rest following work. Heart rates were obtained for a continuous EKG. In addition, several measurements of pulmonary function were performed: pulmonary diffusing capacity (DL_{CO}), inspiratory capacity, inspiratory reserve volume, expiratory reserve volume, tidal volume, vital capacity, minute ventilation, airway resistance, respiratory frequency, functional residual capacity, residual volume, and total lung capacity.

Following CO inhalation, a level of 3.95 ± 1.87 percent COHb was obtained, compared with 3.5 ± 1.8 percent COHb observed in the group of smokers used as controls. Individual data on oxygen uptake and oxygen debt before and after inhalation are shown in Table 8–6. Following CO inhalation, no significant change was observed in the mean oxygen uptake, although there was a statistically nonsignificant increase in the mean oxygen debt. There was a significant increase when the oxygen debt was related to the total increased oxygen uptake. The mean oxygen debt ratio increased 14 percent, from 0.213 to 0.243 ($p < 0.05$). The mean heart rate was significantly less after inhalation of CO, both at rest and during exercise (Table 8–7). There was a statistically significant decrease in the mean DL_{CO} at rest after inhalation of CO ($p < 0.05$), although all values remained within normal limits. The difference was not apparent during exercise. In pulmonary function studies, significant changes ($p < 0.05$) occurred in inspiratory capacity, total lung capacity, and maximal voluntary ventilation (Table 8–8). These findings could partially represent the effects not related to CO exposure, since sham exposure and double-blind technique were not used.

b. *Studies of Hemodynamic Responses*

Changes in gas exchange following exposure to CO are dictated by changes in the O_2Hb dissociation curve in the presence of various concentrations of COHb, as is illustrated in Figure 8–1. Because the dissociation curve is shifted to the left, maintenance of the pre-exposure arterio-venous oxygen difference and oxygen delivery requires that the venous oxygen tension be decreased. This decrease in mixed venous oxygen tension has been shown to occur experimentally by Ayres[62] et al. Cardiorespiratory responses of five subjects to brief exposures of relatively high levels of CO were determined by transvenous catheterization of the heart. Intracardiac pressures and

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*The *oxygen debt* (O_{2D}) = $O_2^2 - O_2^1$, where O_2^1 is the oxygen uptake during a resting period before exercise and O_2^2 is the increased oxygen uptake after exercise has ceased. Because of the individual differences in the increase of oxygen uptake with exercise, the oxygen debt may also be expressed as a ratio.

Table 8–6. TOTAL INCREASED OXYGEN UPTAKE ($\dot{V}_{O_2}$), OXYGEN DEBT (O_{2D}), AND RATIO OF O_{2D} TO $\dot{V}_{O_2}$ BEFORE AND AFTER CO INHALATION BY TEN NONSMOKERS[61]

Subject	Before CO inhalation			After CO inhalation		
	$\dot{V}_{O_2}$, ml of O_2	O_{2D}, ml of O_2	$O_{2D}/\dot{V}_{O_2}$	Work $\dot{V}_{O_2}$, ml of O_2	O_{2D}, ml of O_2	$O_{2D}/\dot{V}_{O_2}$
1	5520	1240	0.183	5940	1060	0.151
2	6160	2530	0.295	5940	2680	0.310
3	5840	1000	0.146	5660	1900	0.251
4	6080	1360	0.183	5920	1040	0.174
5	5840	1800	0.236	5200	1840	0.261
6	6160	1480	0.194	6340	2020	0.265
7	6400	1880	0.227	5560	1760	0.240
8	6360	2040	0.243	5860	1860	0.240
9	5680	1660	0.226	5880	2420	0.291
10	5860	1440	0.196	5640	1840	0.246
Mean	5990	1648	0.213	5794	1842	0.243
SD	±290	±452	± 0.042	± 301	±510	±0.48
p				<0.10	<0.20	<0.05

Table 8–7. HEART RATE AND PULMONARY DIFFUSING CAPACITY (DL_{CO}) BEFORE AND AFTER CO INHALATION BY TEN NONSMOKERS[61]

	Before CO inhalation				After CO inhalation			
	Rest	2 min. exercise	5 min. exercise	3 min after exercise	Rest	2 min. exercise	5 min. exercise	3 min. after exercise
Heart rate, beats/min. Mean S D p	90.0 ±8.9	137.8 ±9.7	143.6 ±11.0	102.4 ±13.5	82.0 ±7.2 <0.01	129.2 ±8.7 <0.02	135.8 ±11.3 <0.01	94.8 ±14.1 <0.10
DL_{CO}, ml/min x mm Hg Mean S D p	33.9 ±5	45.4 ±7	48.3 ±8	37.4 ±6	31.3 ±3 <0.05	45.5 ±6	46.3 ±8	36.7 ±5

Table 8–8. MEAN PULMONARY FUNCTION STUDIES BEFORE AND AFTER CO INHALATION BY TEN NONSMOKERS[61]

	Before	*After*	*Direction of change*	*p*
Inspiratory capacity, ml	3655 ± 415	3380 ± 419	-	<0.05[a]
Inspiratory reserve volume, ml	2745 ± 606	2580 ± 650	-	<0.02
Expiratory reserve volume, ml	2075 ± 799	2155 ± 788	+	<0.60
Tidal volume, ml	915 ± 352	805 ± 482	-	<0.20
Vital capacity, ml	5820 ± 740	5530 ± 740	-	<0.10
Residual volume, ml	1975 ± 524	2010 ± 495	+	<0.80
Total lung capacity, ml	7705 ± 1083	7545 ± 993	-	<0.02[a]
Functional reserve capacity, ml	4050 ± 1100	4160 ± 930	+	<0.46
Max. breathing capacity, liter/min.	175 ± 23	185 ± 27	+	<0.05[a]
Max. expiratory flow rate, liter/min.	585 ± 60	590 ± 53	+	<0.50
Airway resistence, cm H_2O/liter-min.	0.89 ± 0.22	1.06 ± 0.62	+	<0.40

[a] Differences statistically significant.

mixed venous blood samples were obtained by using a cardiac catheter positioned in the main pulmonary artery. Arterial blood was sampled from a brachial artery. Oxygen tensions were measured before, and 5 to 7 minutes after, inhalation of 0.4 percent (4,600 mg/m^3 or 4,000 ppm) CO in air. The data are shown in Table 8–9. Oxygen tensions of arterial and mixed venous bloods decreased an average of 7.3 and 13.3 percent, respectively, when the COHb rose to between 5 and 10 percent. The difference in arterial and venous blood, which reflects extraction of oxygen by the tissues, increased in all five subjects. In the fifth subject, who received the greatest amount of CO, the left atrial pressure rose and the cardiac output fell, indicating development of abnormal left ventricular function (such changes occur with the onset of congestive heart failure). Intracardiac pressures, cardiac output, oxygen consumption, and ventilation did not change in the remaining four subjects.

Ayres[63] et al. have also reported on a study of 26 patients, each of whom had a catheter placed in the ascending aorta and pulmonary artery. Samples of mixed expired air and arterial, mixed venous, and coronary sinus (venous) blood were obtained before exposure. The subjects breathed a mixture of 5 percent (57,000 mg/m^3 or 50,000 ppm) CO in air for a period of 30 to 120 seconds. Ten minutes after exposure, repeat samples of blood and mixed expired air were collected while the subjects breathed room air. Coronary blood flow was measured immediately before and 10 minutes after exposure.

Table 8–10 shows mean values for selected cardiorespiratory measurements in the 26 subjects before and after CO inhalation. The significant increase ($p < 0.01$) in average

Table 8–9. HEMODYNAMIC AND RESPIRATORY RESPONSES OF FIVE SUBJECTS TO CO INHALATION[62]

Subject	COHb, %	Pressure, mm Hg				A-V diff[e] percent by volume	Cardiac output, liters/min.	Vent,[f] liters	$P^g_{CO_2}$, mm Hg
		LA[a]	PA[b]	P_{aO_2}[c]	P_{vO_2}[d]				
1–									
Before	0.48	28	9	89	45	3.40	5.23	4.23	34
After	8.84	28	9	81	42	3.82	4.46	4.23	36
2–									
Before				86	37	3.96	4.37	4.68	36
After	6.29			80	30	4.55	4.35	5.72	36
3–									
Before		3	14	74	42	3.92	4.31	2.55	36
After		3	12	68	37	4.24	4.17	3.11	40
4–									
Before	0.37	9	13	84	49	4.00	5.32	5.43	39
After	4.95	9	13	79	42	4.66	6.54	7.36	38
5–									
Before	0.96	7	12	77	41	4.02	6.00	4.87	36
After	9.69	11	18	72	35	4.81	4.68	4.24	39

KEY:

[a]LA = Left atrium (wedge).
[b]PA = Pulmonary artery (mean).
[c]P_{aO_2} = Arterial oxygen tension.
[d]P_{vO_2} = Mixed venous oxygen tension.
[e]A-V diff = Arterial-venous difference.
[f]Vent = Ventilation per square meter of body surface area per min.
[g]P_{CO_2} = Carbon dioxide tension.

oxygen extraction ratio indicates a more complete extraction of oxygen from perfusing arterial blood in the presence of increased COHb. There was a mean decrease of 20 percent in the venous oxygen tension, and this can be associated with the increase in COHb concentration. This decrease implies a similar decrease in tissue oxygen tension and suggests the possibility that some cellular processes that are particularly sensitive to oxygen tension could have been inactivated. The decrease in the mixed venous oxygen tension was regarded as a major primary response to CO inhalation, and Ayres believes that other hemodynamic changes must be considered as secondary. The associated increases in cardiac output were considered a compensatory mechanism for tissue hypoxia, since they resemble the physiologic response to hypoxemia.

Peripheral tissues normally extract about 25 percent of the oxygen present in arterial blood; the remaining 75 percent serves as a reserve supply for increased oxygen needs. The mixed venous oxygen tension is normally about 40 mm Hg, but during exercise it may drop to 20 mm Hg. In contrast, the myocardial oxygen requirements are such that, even at rest, 75 percent of the oxygen is extracted from the coronary circulation. Coronary venous blood is, therefore, only about 25 percent saturated, corresponding to an oxygen tension of about 20 mm Hg. No substantial reserve of oxygen is available to tissue supplied by the coronary vasculature unless the coronary artery dilates in response to low oxygen tensions. The coronary circulation is thus capable of increasing the flow rate in response to increased oxygen needs, rather than increasing the percent of oxygen extraction. Coronary vascular disease, however, may prevent an increase in coronary blood flow in response to need, and the myocardium may be forced to attempt to extract more oxygen at the expense of an already reduced coronary venous and tissue oxygen tension.

The responses of the myocardium to increased oxygen requirements induced by CO inhalation in patients both with and without coronary disease have also been studied by Ayres[63] et al., by means of an additional parameter to measure the response to CO. During periods of insufficient oxygen supply, the citric acid (Krebs') cycle, important in glucose metabolism, is impaired; the utilization of pyruvate produced by glycolysis is decreased, and results in an accumulation of pyruvate in the cytoplasm and the resultant transformation of pyruvate into lactate. Increasing cellular concentrations of lactate and pyruvate decrease in normal extraction of these metabolites from the coronary blood. The extraction ratio of either lactate or pyruvate (the arterio-coronary sinus difference divided by the arterial concentration) can thus be a useful index for expressing oxidative metabolism; these parameters are relatively independent of arterial concentrations. The extraction ratios for both metabolites range from 15 to 30 percent when oxygen is plentiful. During periods of inadequate oxygenation, however, extraction decreases, and lactate and pyruvate may actually be produced by the myocardium. Under these conditions, coronary sinus concentrations exceed arterial concentrations.

Myocardial metabolic studies were conducted on seven patients with noncoronary heart disease and four patients diagnosed as having coronary artery disease. All patients had a catheter placed in the proximal coronary sinus. The data from this study are shown in Table 8–11. In contrast to the systemic gas exchange studies, the oxygen extraction decreased for both groups and could be correlated with an increase in COHb. The oxygen extraction ratio also decreased in each of the two groups (cf. an increase in the systemic studies). Coronary blood flow increased significantly in the patients with noncoronary heart disease, but did not in those with coronary heart disease. Lactate extraction ratios changed to production in both groups, but the change was statistically significant only for the patients with coronary heart disease. Figure 8–12 shows the responses of three representative subjects, one with coronary artery disease, one with mitral stenosis, and a third with emphysema. Changes similar to those already described occurred in the patients with mitral stenosis and coronary artery disease. The emphysematous patient was hypoxemic at rest (PaO_2 = 47 mm Hg); and, when the COHb level increased 6 to 7 percent, there was an increase in coronary blood flow and a drop in the mixed venous and coronary sinus oxygen tensions from 20 and 20 mm Hg to the extremely low levels of 12 and 2 mm Hg, respectively. It can be noted from the examination of Table 8–11 that the average blood COHb concentrations of all 11 subjects at the time these effects were measured were about 8.5 to 9 percent. From examination of Figure 8–12, however, it can be noted that at least two representative patients had blood COHb levels considerably lower than the average (cf. 5.58 percent COHb levels above 5 percent, such as those disease and 6.37 percent COHb in the patient with emphysema).

From these studies, it would appear that persons with coronary heart disease and emphysema may be particularly susceptible to exposures of CO that could lead to blood COHb levels about 5 percent, such as those that may be encountered in smoking or, less frequently, in community air pollution. Because in this experiment there was only a brief exposure to very high CO levels, the observed effects are difficult to relate to equilibrium conditions or longer exposures.

Both of Ayres' studies[62,63] show that increased COHb lowers the arterial oxygen tension (Tables 8–9 and 8–10). The more recent

Table 8–10. SYSTEMIC CARDIORESPIRATORY MEASUREMENTS IN 26 SUBJECTS BEFORE AND AFTER CO INHALATION[63]

Measurements	Control mean	CO mean	F[a]	p[b]
COHb, percent	0.98	8.96		
Arterial P_{O_2}[c], mm Hg	81	76	22.1	<0.01
Venous P_{O_2}, mm Hg	39	31	94.5	<0.001
Arterial P_{CO_2}[d], mm Hg	40	38	4.2	<0.05
Ventilation, liters/min.	6.86	8.64	4.1	<0.05
Cardiac output, liters/min.	5.01	5.56	4.4	<0.05
Oxygen extraction,[e] ml/100 ml	4.30	4.56	2.7	<0.20
Oxygen extraction ratio[f]	0.27	0.32	31.2	<0.01
Alveolar-arterial O_2 difference	20	29	7.0	<0.05

[a] F = variance ratio calculated for paired data with interaction as denominator.

[b] p = probability that observed difference between control and CO means is due to chance.

[c] P_{O_2} = oxygen tension.

[d] P_{CO_2} = carbon dioxide tension.

[e] Oxygen extraction = arteriovenous oxygen content difference.

[f] Oxygen extraction ratio = oxygen extraction divided by arterial oxygen content.

one[63] also shows that the alveolar-arterial oxygen difference ($A\text{-}aD_{O_2}$) is increased (Table 8–10); this difference is an index of the inefficiency of oxygen transfer from the lungs to the blood. Brody and Coburn[64] have recently shown, both theoretically and experimentally, that under some conditions an increased $A\text{-}aD_{O_2}$ results from changes in the sigmoid shape of the O_2Hb dissociation curve induced by CO. These investigators have calculated the effect of 0 to 50 percent COHb on the $A\text{-}aD_{O_2}$ under conditions of veno-arterial shunting and ventilation and perfusion imbalance, and have compared this to the effect of an equivalent degree of anemia (which does not alter the sigmoid shape of the O_2Hb dissociation curve). The results have indicated that an increase of 10 percent in the COHb causes an increase in the $A\text{-}aD_{O_2}$ in the presence of shunts as small as 2 percent of the cardiac output, but there were no significant changes when the shunts were less than 1 percent of the cardiac output. The effect of an equivalent anemia was considerably less. The changes in $A\text{-}aD_{O_2}$ with perfusion abnormalities were smaller than those with veno-arterial shunts, the effect of an equivalent anemia being less than that of increased COHb. The results of these calculations were verified experimentally by exposing five normal subjects, two patients with intracardiac shunts, and two patients with perfusion imbalance to sufficient CO to give an increase in COHb of about 10 percent. These results are tabulated in Table 8–12. Brody and Coburn consider that their findings have important implications, since the tissue hypoxia produced by increased COHb may be augmented by arterial hypoxemia in the presence of abnormal perfusion relationships or veno-arterial shunts. Arterial hypoxemia may play an important role in CO-poisoning

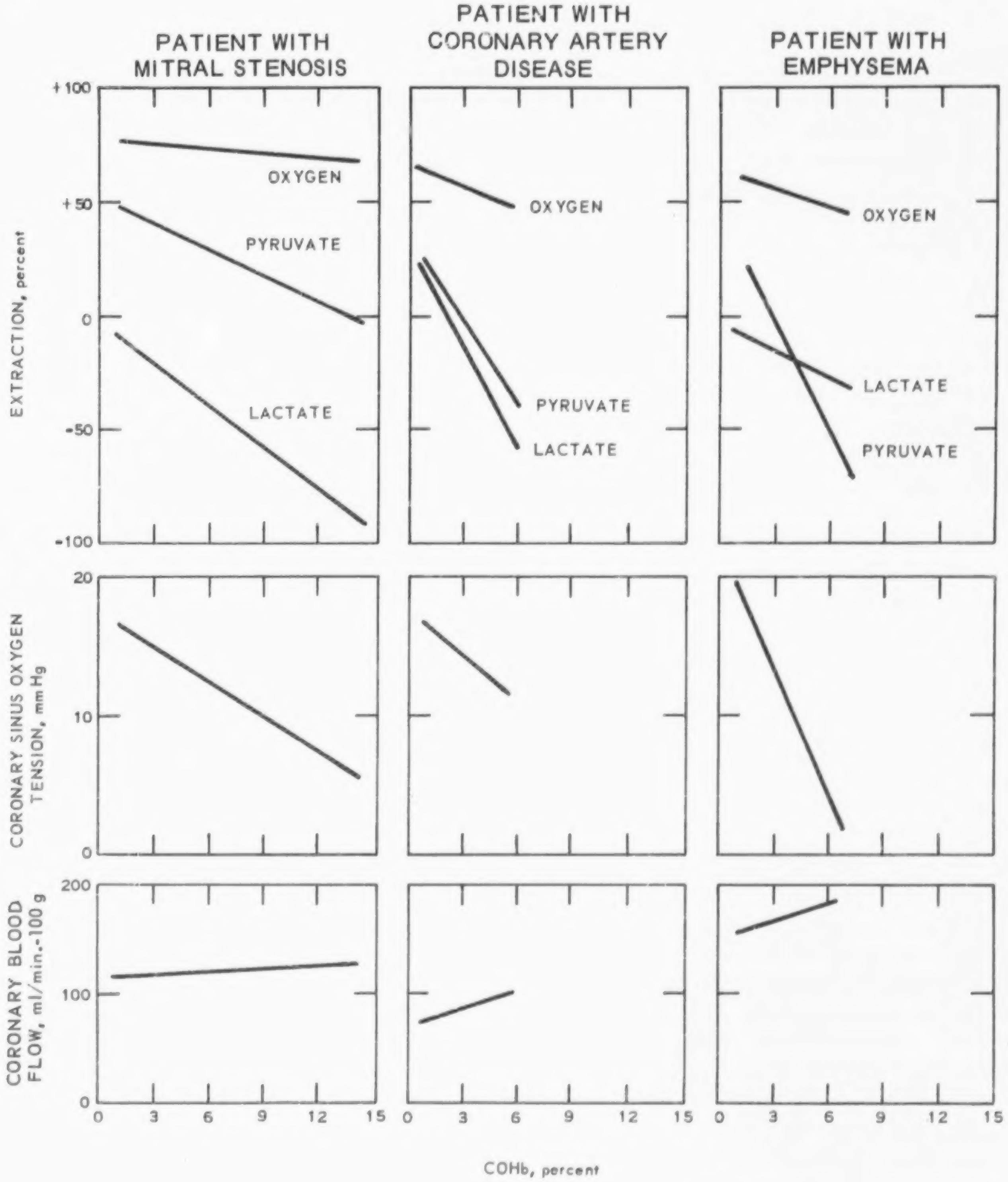

Figure 8-12. Myocardial metabolic measurements in three representative patients before and after CO inhalation.[63]

Table 8–11. MYOCARDIAL METABOLIC MEASUREMENTS IN 11 SUBJECTS BEFORE AND AFTER CO INHALATION[63]

Measurements	Control mean	CO mean	F[a]	p
Group 1 – non-coronary heart disease (7 patients)				
COHb, %	0.95	9.00		
Q_M,[b] ml/min - 100 g	129	186	6.5	<0.05
Oxygen extraction,[c] ml/100 ml	11.84	8.89	52.7	<0.001
Oxygen extraction ratio[d]	0.75	0.64	42.1	<0.001
MVO_2,[e] ml/min - 100 g	14.3	15.9	0.4	
P_{csO_2},[f] mm Hg	21	17	2.9	<0.20
Lactate extraction ratio[d]	-0.01	-0.19	0.7	
Pyruvate extraction ratio[d]	0.28	0.24	0.3	
Group 2 – coronary heart disease (4 patients)				
COHb, %	0.66	8.69		
Q_M, ml/min - 100 g	102	127	0.5	
Oxygen extraction, ml/100 ml	12.71	8.82	34.7	<0.01
Oxygen extraction ratio	0.75	0.58	419	<0.01
MVO_2, ml/min - 100 g	12.9	11.3	0.5	
P_{csO_2},[f] mm Hg	19	17	12.9	<0.05
Lactate extraction ratio	0.12	-0.36	19.6	<0.05
Pyruvate extraction ratio	0.39	-0.07	25.6	<0.05

[a] F = variance ratio calculated for paired data with interaction as a denominator.

[b] Q_M = coronary blood flow.

[c] Oxygen extraction = arterio-coronary sinus oxygen difference.

[d] Oxygen, lactate, and pyruvate extraction ratios = respective extraction divided by arterial concentration.

[e] MVO_2 = myocardial oxygen consumption.

[f] P_{csO_2} = coronary sinus oxygen tension.

of subjects with normal lungs if they develop perfusion imbalance or veno-arterial shunts when unconscious. Persons with these abnormalities may therefore face unusual risks from exposure to CO.

G. NONHEMOGLOBIN ABSORPTIVE SYSTEMS

1. Myoglobin

Myoglobin is structurally related to hemoglobin, and hence can be expected to react with CO in a manner similar to hemoglobin. Because myoglobin contains only 1 heme per molecule, the reaction occurs without the formation of intermediates. *In vivo,* its function may be to act as a reservoir for oxygen within the muscle fiber, serving to tide the muscle over from one contraction to the next.

Two studies of the interaction between CO and myoglobin have been undertaken, one employing human myoglobin *in vitro,* and the other with dogs. Rossi - Fanelli and Antonini have recently studied the oxygen and CO equilibria of human myoglobin *in vitro.*[65] The oxygen dissociation curve of human myoglobin was found to be hyperbolic. It differs from that of hemoglobin in that it is not affected by the hydrogen-ion concentration, the ionic strength, or the concentration of myoglobin. Both the shape and the properties of the oxymyoglobin (O_2Mb) dissociation curve reflect the difference in structure and function between myoglobin and hemoglobin. Although the relative affinity of myoglobin for CO is not as high as that of hemoglobin, it is still sufficient to cause appreciable formation of carboxymyoglobin (COMb) in nonfatal CO poisoning.

The proportion of inhaled CO that binds to myoglobin has been studied in dogs by Luomanmäki.[66] In the calculation of his results, Luomanmäki assumed that the CO was equilibrated between an intravascular and an extravascular pool, and that the latter was comprised mostly of myoglobin. The extravascular CO capacity was determined from the difference between the separately measured total body CO capacity and the intravascular CO capacity. The total body CO capacity was determined using the dilution principle. A known amount of CO was injected into the inspiratory tube of a rebreathing system. The increase in blood COHb was measured at intervals, and total body CO capacity was calculated as follows:

$$\text{Total body CO capacity (ml STPD)} = \frac{\text{Injected CO (ml STPD)} \times 100}{\text{Increase of blood COHb}}$$

The equation assumes that the increase in COHb is estimated at the time when there is no more net transfer between the different CO pools. The measured COHb levels must be extrapolated to the time of CO injection to correct for any increase in COHb due to endogenous production of CO.

Data relating COHb values to extravascular CO capacities, half-times, and equilibrium time of CO transfer from the intravascular to the extravascular pool are shown in Table 8–13. The mean extravascular CO capacity was 22.9 percent of the total body CO capacity. There was no significant linear correlation between the extravascular CO capacities and the COHb levels, although only 3 of the 11 dogs had COHb levels exceeding 10 percent. The mean of the half-time to equilibrium between the two pools was 12.5 minutes, and the mean of the equilibrium times was 29.2 minutes. There was no linear correlation between either the half-time or the equilibrium time and the COHb level. The transfer of CO from the intravascular to the extravascular CO pool occurs within the time needed for circulatory mixing, as detected by ^{51}Cr-labeled red cells. The distribution of CO between intravascular and extravascular CO pools was independent of P_{O_2} in the P_{O_2} range of 65 to 440 mm Hg.

Table 8–12. EFFECT OF CO ON ALVEOLAR-ARTERIAL OXYGEN DIFFERENCE (A-aD_{O_2}) IN NINE SUBJECTS AFTER EXPOSURE SUFFICIENT TO INCREASE COHb ABOUT 10 PERCENT[64]

Subject	COHb, %			A-aD_{O_2}, mm Hg		
	Initial		Final	Initial		Final
Normal subjects (5)	0.9		11.7	12.1		11.6
S D	±0.1		±4.7	±4.9		±5.9
p value		<0.005			>0.5	
Intracardiac shunts						
Subject 1	2.1		12.8	36.5		46.9
Subject 2[a]	1.0		12.7	56.7		62.8
Perfusion imbalance						
Subject 3	2.1		12.8	38.0		41.0
Subject 4	1.7		11.5	39.8		42.6

[a] 2,3-diphosphoglycerate was elevated in this patient, which suggests that the O_2Hb dissociation curve was shifted to the right. This shift might, in part, counteract the effect of COHb on the A-aD_{O_2}.

Table 8–13. EXTRAVASCULAR CO CAPACITIES, HALF-TIMES, AND EQUILIBRIUM TIMES FOR TRANSFER OF CO FROM INTRAVASCULAR POOL TO EXTRAVASCULAR POOL, AND LEVELS OF BLOOD COHb AT END OF TRANSFER[66]

Dog No.	Extravascular CO capacity, % of total body CO capacity	Half-time of CO transfer, minutes	Equilibrium time of CO transfer, minutes	COHb,[a] %	Body weight, kg	Body myoglobin content, g	Body myoglobin content, g/kg body wt
1	14.6	14	35	5.35	12.9	28.4	2.20
5	29.0	9	19	10.50	15.0	60.0	4.00
6	20.9	18	45	0.75	15.9	44.0	2.77
7	17.5	12	30	30.95	16.4	35.8	2.18
9	16.0	12	28	1.16	15.5	35.1	2.26
10	16.3	14	33	7.42	15.9	32.8	2.06
11	15.6	8	17	35.00	15.0	26.9	1.79
12	31.8	8	15	2.54	13.2	55.2	4.18
14	37.5	8	22	2.32	10.6	36.6	3.45
18	27.5	17	40	2.42	17.5	83.5	4.77
21	26.0	17	37	5.00	13.6	46.3	3.40
Mean	22.9	12.5	29.2	–	14.68	44.05	3.01
S D	7.4	3.7	9.4	–	–	–	0.98

[a] COHb values extrapolated to the time of CO injection because of endogenous formation of CO.

2. Cytochrome Oxidases

Cytochrome oxidases are hemoproteins that, *in vitro*, are capable of reacting with CO. The reaction between the heme moiety of these compounds and CO appears to be similar to the reaction of CO with hemoglobin and myoglobin. Reversible binding, photolysis, and competition between oxygen and CO are characteristics of cytochrome oxidases. Nevertheless, the evidence at this time suggests that interactions between CO and cytochrome oxidases in the mammalian cell are of minor significance when compared to the effects of CO on hemoglobin and myoglobin.

Although all three types of cytochrome oxidases that are important in the oxygen consumption system of the mammalian cell can be blocked in some part by CO, only the terminal member of the electron transfer system (which is located in the mitochondria) combines with CO; the other members do not combine unless they are denatured. This terminal member is known as cytochrome a_3 .

The reaction between cytochrome a_3 and oxygen accounts for about 90 percent of the total oxygen consumption by the cell. In the presence of oxygen, the reaction of CO with cytochrome a_3 is competitive, and the CO uptake depends on the concentration of the enzyme and the ratio of CO to O_2, rather than on the concentration of CO alone. For 50 percent inhibition, the required ratio of CO to O_2 is between 2.2 and 28.[67-69] Because the ratio is usually so much lower, these conditions give oxygen a substantial advantage in competition with CO.

A more likely candidate for CO inhibition *in vivo* is cytochrome P-450. The latter, located in the microsomal fraction of the cell, is the terminal member of the chain of mixed function oxidases that catalyze the incorporation of atmospheric oxygen into organic compounds and for such reactions as the hydroxylation of acetanilide, demethylation of codeine, and hydroxylation of 17-hydroxyprogesterone at carbon-21. The experimental evidence that the CO-binding pigment of the microsomes is in the terminal oxidase of mammalian tissues was provided by Cooper[70] et al. These investigators reported that the ratio of CO to O_2 required for 50 percent inhibition is approximately 1 to 1 (range 0.5 to 1.5).

All of the above data were obtained *in vitro*. Whether similar events occur *in vivo* is uncertain. Root[71] considers that at a P_{CO} compatible with life, only nonsignificant blocking of the oxygen consumption systems occurs. Although the P_{CO} in the cell never exceeds a few tenths of a mm Hg before fatal blocking of hemoglobin occurs, the intracellular P_{O_2} is also low. Forster[72] estimates the intracellular P_{O_2} to be about 1 mm Hg in the mitochondrial region. *In vitro*, the minimum P_{O_2} for isolated mitochondrial function is 0.5 mm Hg. At equilibrium, 1,150 mg/m^3 (1,000 ppm) CO should result in a P_{CO} of approximately 0.7 mm Hg in the blood. The gradient, if any, in P_{CO} from the erythrocyte to the intracellular organelles is unknown. Even if there is a complete transfer of CO to an intracellular locus, however, concentrations of CO commonly found in community air pollution are likely to be of little relevance concerning either cytochrome a_3 or cytochrome P-450. In terms of the total distribution throughout the body of an inhaled dose of CO, the amounts bound to these hemoproteins are small when compared with hemoglobin and myoglobin.

Most of the useful information concerning the distribution of CO in the body has been summarized by Coburn[73] et al. Figure 8–13 is a diagrammatic representation of the factors influencing body CO stores.

H. EFFECTS OF CARBON MONOXIDE AT HIGH ALTITUDE

The effects of CO and of hypoxia induced by high altitude are similar. Most experimental data suggest that when high altitude and CO exposures are combined, the effects are additive. *In vivo*, there is an interaction between the two factors so that exposure to one may induce a physiological response that influences the response of the body to the other. For example, Forbes et al. have shown

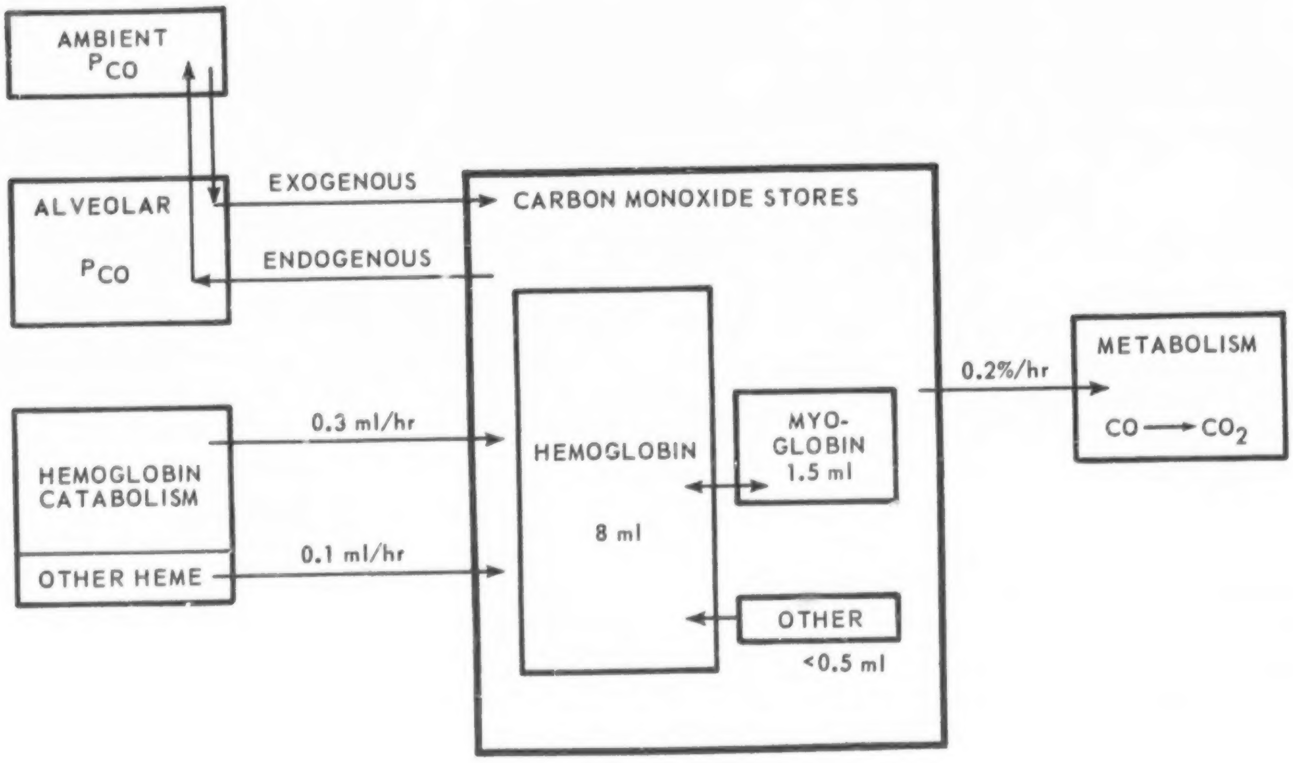

Figure 8-13. Diagramatic summary of current concepts regarding variables that influence body CO stores.[73]

that during light activity, their subjects had an increased rate of CO uptake at an altitude of 16,000 feet compared to that at sea level, because of the hyperventilation that results from the decreased P_{O_2}.[29] When the ventilation rate was corrected to its value at sea level, the rate of uptake of CO decreased to a value within 10 percent of the sea level value.

Although the effects of hypoxia and CO appear to be additive, individually they do seem to provide different physiological responses. This is because they have different effects on blood P_{O_2}, on the affinity of O_2 for blood hemoglobin, on the extent of O_2Hb saturation, and on ventilation. The presence of COHb increases the affinity of hemoglobin for O_2, but lowers the total O_2Hb saturation. The ventilation rate appears to be influenced by receptors in the carotid and aortic bodies that are responsive to blood P_{O_2} and P_{CO_2}.[71] Hypoxia results in a lowering of the P_{O_2} and increased ventilation ensues; in CO exposure, the P_{O_2} apparently does not change sufficiently to induce the necessary increased ventilation.

Several different physiological and psychomotor tests have been used to determine the effects of altitudes with and without CO. Pitts et al. have observed the physiological responses to exercise when blood COHb levels were increased by 6 percent and 13 percent in a group of ten men at simulated altitudes (sea level, 7,000, 10,000, and 15,000 feet).[74] The parameters measured were pulse rate, respiratory rate, and minute ventilation. A previous study had indicated that in subjects at rest, the pulse showed no change with altitude up to 16,500 feet. After regulated exercise at altitudes from sea level up to 21,000 feet, however, it showed a steep, almost linear, increase. Of the parameters measured in both these studies, mean pulse rate during exercise and for the 5 minutes immediately following exercise showed the closest correlation with blood COHb and ambient P_{O_2}. At sea level, an increase of 13 percent in COHb increased the mean excercise pulse rate from 105 to 112 and the recovery pulse rate from 91 to 98. An increase of 6 percent COHb had no effect at sea level; at 7,000 feet, however, an increase of 6 percent COHb produced a significantly higher exercise pulse rate compared to that produced by altitude alone. Pitts calculated that for every 1 percent increase in blood COHb in normal subjects, up to 13 percent COHb, the increase in exercise pulse rate is equal to that which would be produced by a 335-foot rise in altitude throughout the range 7,000 to 10,000 feet. It is likely that some of the subjects were smokers, since the group mean control COHb level ranged from 2.88 to 3.64 percent on different days. Since the smokers would have been preconditioned in part to the effects of CO, their responses to additional small quantities of CO might be expected to be lowered. This could have masked the additive effect of CO and hypoxia.

A more recent study has compared the effects of CO exposure and altitude.[75] Eight healthy male subjects were divided randomly into two groups of four each; each group followed a different daily schedule. The subjects were briefly exposed daily for 10 days to concentrations of 5 percent CO (57,500 mg/m^3 or 50,000 ppm) at 4-hour intervals between the hours of 7 a.m. and 11 p.m. The doses were sufficient to give an average COHb level of 15 percent, although values ranging between 5 and 25 percent were recorded. A variety of circulatory, ventilatory, and renal function tests were performed during the course of the experiment. The same experimental protocol was also carried out on the same eight subjects after spending 10 days at an altitude of 11,225 feet. This altitude gave roughly, a degree of hypoxemia equivalent to that given by 15 percent COHb. The data obtained from the two studies are compared in Table 8–14. Of great significance are the circulatory and ventilatory responses to the two types of hypoxic conditions. As expected, CO hypoxemia shifted the O_2Hb dissociation curve to the left, whereas high altitude caused a shift to the right, the latter occurring during the first 24 hours. At increased altitude, both the cardiac output and the ventilatory rate increased within the first 24 hours, whereas CO had no consistent effect on these parameters.

The lowered arterial P_{O_2} at high altitude most likely stimulated the chemoreceptors in the aortic and carotid bodies, with the resultant regulatory changes in ventilation. Mills and Edwards[76] have recently shown that these chemoreceptors are also stimulated during CO inhalation. These investigators have suggested that the lack of ventilatory response during CO hypoxemia is a result of depression of respiratory centers in the central nervous system. The effects of the two types of hypoxemia at the cellular level can be estimated by comparing the P_{O_2} of the mixed venous blood under both circumstances, since this reflects tissue P_{O_2}. The data in Table 8–14 show that the average P_{O_2} of mixed venous blood in CO hypoxemia is lower than in hypoxic (high altitude) hypoxemia. In both types of hypoxemia, a lowered tissue P_{O_2} is expected; as indicated by the mixed venous P_{O_2}, this is more pronounced in CO hypoxemia. At increased altitude, the shift of the O_2Hb curve to the right and the circulatory and ventilatory responses compensate for most of the associated tissue hypoxia during the first 24 hours. Such regulatory mechanisms do not appear to be stimulated by CO hypoxemia, and hence the latter may be considered to be more of a physiological burden.

Other studies on the combined effects of CO and altitude have used psychomotor tests. Variable results have been reported, but some of these may be explained by the use of different tests and others by the lack of proper controls. The flicker fusion frequency (FFF) and the critical flicker fusion (CFF), often employed in these studies, have recently been criticized because of their lack of reliability.[77]

McFarland[50] et al. have used the increased threshold of visual perception as an index of the effect of both CO and high altitude.

Table 8-14. AVERAGE DATA FOR EIGHT SUBJECTS (DIVIDED INTO TWO GROUPS OF FOUR) TO COMPARE EFFECTS OF CO AND HIGH ALTITUDES ON VARIOUS PHYSIOLOGICAL PARAMETERS[75]

Test	Effect of 15% COHb	Effect of 11,225-ft altitude
O_2Hb saturation curve	Shift to left	Shift to right
Affinity of Hb for O_2	Increased (within 12 hr)	Decreased (within 24 hr)
Mixed venous oxygen tension, by estimation	10 to 20% decrease throughout exposure period	20% increase on first day, 10% decrease on second day, return to normal for rest of experimental period
Ventilation		
$\dot{V}_E STPD^a$ - rest	No change	15 to 20% decrease
- work	Slight increase on first day	Slight decrease
$\dot{V}_E BTPS^b$ - rest	No change	30% increase
- work	No systematic change	35% increase on first day; 50% increase by tenth day
Respiratory rate - rest	No change	15 to 35% increase
- work	No change	15 to 35% increase
Circulation		
$P_{aCO_2}{}^c$ - rest	Almost unchanged	Continuous decrease from 90 to 75% of control
$P_{vCO_2}{}^d$ - rest	Almost unchanged	Continuous decrease from 90 to 75% of control
Cardiac output	Group 1 increased 27% on first day, followed by return to normal; no change in Group 2	Group 1 increased 35 to 45% for the entire 10-day period; Group 2 increased 25% by fourth day and returned to normal by end of stay
Mixed venous-arterial CO_2 difference, by estimation - rest	Group 1 decreased 20% on first day; Group 2 showed no change	Group 1 decreased 15 to 20% for the entire 10-day period; Group 2 decreased on fourth day only
- work	Group 1 increased 20% percent on third and fifth days; no other changes noted	15 to 25% increase for the entire 10-day period
Renal function		
Glomerular filtration	50% increase on first day, return to normal on second day, remain within 20% of control for rest of experimental period	Very slight decrease, but close to control value

Table 8-14 (continued). AVERAGE DATA FOR EIGHT SUBJECTS (DIVIDED INTO TWO GROUPS OF FOUR) TO COMPARE EFFECTS OF CO AND HIGH ALTITUDES ON VARIOUS PHYSIOLOGICAL PARAMETERS

Test	Effect of 15% COHb	Effect of 11,225-ft altitude
Renal plasma flow	40% increase on first day, return close to pre-exposure value on second day, remain < 15% below control value for rest of experimental period	Very slight decrease, but close to control value
Diuresis	Increase of 400 to 500 ml	Increase to more than twice control by sixth day
Serum lipids (cholesterol)	No significant change for first 4 days; 6% increase in last 2 days ($p < 0.05$)	6 to 9% increase in first 2 days
Hematocrit	No change	Very slight increase (43.5 to 47)
Reticulocyte count	Threefold increase on third day; nearly fourfold increase by sixth day	Twofold increase on third day; nearly threefold by ninth day

[a] $\dot{V}_E$STPD (liters/min) - ventilation at 0° C, 760 mm Hg, dry.

[b] V_EBTPS (liters/min) - ventilation at body temperature and ambient pressure saturated with water vapor.

[c] P_{aCO_2} - alveolar carbon dioxide tension.

[d] P_{vCO_2} - mixed venous carbon dioxide tension.

Although studies of visual perception have already been discussed in Section E.2, it is pertinent to note at this point that McFarland et al. documented an impairment in visual perception in a single subject with a COHb of about 5 percent at sea level that was equivalent to the impairment associated with the low P_{O_2} at an altitude of 7,000 feet.

In another experiment, a group of four trained subjects was used to study the time course of recovery from CO and altitude.[52] Data from a single subject suggest that it takes longer to recover from a given COHb level than from an equivalent lowering of P_{O_2} due to altitude. The difference could not be accounted for wholly by the presence of COHb. It is possible that the compensatory mechanisms normally activated by lowered P_{O_2} were not activated when CO caused the drop in O_2Hb saturation. Alternatively, it is also possible that CO exerts a specific toxic effect on the central nervous system that is unrelated to the COHb level.

In both studies just described, the investigators imply that the subjects exhibited similar responses, but they do not supply supporting data. Other investigators have commented on the great variability in response between subjects when similar tests have been used.

Lilienthal[78] et al. demonstrated an impairment in FFF in five subjects at altitudes of 10,000 to 12,000 feet. The combined exposure to CO (COHb increases of 5 to 9 percent) and an altitude of 5,000 to 6,000 feet produced an impairment in FFF, although neither of these stresses alone affected the FFF. The data indicate that an increase in the COHb level of 8 to 10 percent above resting values caused the tolerance for altitude to be lowered by 4,000 feet or more. It should be noted that impairment in FFF is not necessarily consistent with a given COHb percentage. For example, at 5,000 feet one subject showed a depressed FFF at 8.7 percent COHb; yet in another experiment at the same altitude, his FFF remained constant at 10.5 percent COHb. There is a possibility that COHb determinations in this experiment were inaccurate. The subjects' resting COHb levels varied from 1.0 to 3.5 percent, indicating that there were smokers in the group. Since smokers may have higher hemoglobin values than nonsmokers,[79] the assumed hemoglobin value used in this experiment may not be valid.

By contrast, Vollmer[80] et al. have found that the effects of CO and altitude are not additive. Twenty subjects were used to study the effect of CO and increased altitude (10,000 and 15,000 feet) on FFF, body sway, and size of the red visual field - all during light activity. Compared with performance at sea level, there was a significant impairment at increased altitude, with and without exposure to CO. There was no significant difference between the mean test scores during hypoxia alone and the mean test scores following administration of CO. The increases in COHb were from 9 to 19 percent, with a final COHb ranging from 12 to 22 percent. This suggests that the resting COHb was 3 percent, and indicates that some of the subjects were smokers. Vollmer suggests that during hypoxia at 15,000 feet, any additional burden imposed by the presence of small amounts of COHb is masked by compensatory mechanisms. Alternatively, he considers that it is possible that 9 to 19 percent COHb does not impose an important additional stress. At 15,500 feet, however, 4 of 17 subjects collapsed after being exposed to CO. The tests used in this study appear inadequate for predicting a serious cardiovascular reaction; nor can their sensitivity be ranked very high.

Most of the above studies were conducted before or during World War II. Recently, Denison[81] demonstrated a significant effect of hypoxia alone on complex reaction times at a simulated altitude of 5,000 feet during light work. At 5,000 feet, eight of ten subjects showed slower reaction times than nine of ten matched controls ($p < 0.05$). This effect of hypoxia was observed only during the early stages of learning the complex experimental task. Once the task had been learned, a simulated altitude up to 8,000 feet had no effect. The effect of small amounts of CO on the learning of a new task at increased altitude remains to be determined.

I. ADAPTATION

A subject may be considered to be adapted (acclimatized) to a new environment when, after repeated or prolonged exposure to that environment, he shows a significant decrease in the amount of reaction experienced per unit intensity of the offending factor without an increase in other types of reaction. Adaptation thus implies some short-range benefit to the organism concerned. Individuals living at high altitude are considered to be adapted to their environment, since it has been shown that they can perform physical labor there which low-altitude residents cannot do as readily at similar elevations. High-altitude inhabitants, however, show a greater incidence of pulmonary hypertension and patent ductus arteriosis,[82] both of which are associated with an increased need to maintain an adequate P_{aO_2}. Thus, not all high-altitude residents are adapted in the formal sense, but they are well compensated. Since most studies of adaptation are of brief duration, the ultimate costs in terms of parameters such as health impairment (i.e., the development of pulmonary hypertension) can easily be overlooked.

Some experimental studies suggest that repeated exposures to low levels of CO result in an adaptation of the subject to additional exposures. In animal studies, the long-term exposure of dogs to low levels of CO for periods of up to 3 months (described in Section F) has resulted in increased hematocrits, hemoglobin, and RBC counts.[54] In studies of heart size after prolonged exposure to CO, cardiac enlargement has been found, presumably reflecting an increased work load on the cardiovascular system.[49] Such changes can be considered as compensatory mechanisms leading to adaptation.

Astrup[83] et al. have demonstrated an increase in hemoglobin concentration in cholesterol-fed rabbits during the first 5 weeks of an 8-week exposure to 195 mg/m^3 (170 ppm) CO. The hemoglobin level then stabilized, but when the CO concentration was increased to 405 mg/m^3 (350 ppm) a further increase in hemoglobin was observed. The compensatory mechanisms that may have been responsible were not discussed by the authors. The degree of visible aortic atheromatosis and the content of total cholesterol in the aortic tissue was significantly higher in the rabbits exposed to CO than in the controls. This factor may be relevant to the pathogenesis of arteriosclerosis in man.

Wilks[84] et al. acclimatized dogs to CO doses ranging from 920 to 1150 mg/m^3 (800 to 1,000 ppm). This resulted in increased RBC, hemoglobin, and blood volume. When these dogs, together with a control group of unacclimatized dogs, were exposed to 575 mg/m^3 (550 ppm) CO for 15 hours, blood levels of COHb were the same in both groups. This suggests that at equilibrium there is no change in CO saturation with increasing hemoglobin.

Russian studies on animals in which hypoxia was created by oxygen deficiency indicate that adaptation may occur through compensations of systems other than the cardiopulmonary system. Such changes include increased myoglobin stores in the tissues, increased vascularization of tissues (especially brain tissue), and changes in the oxygen-consumption of enzyme systems. Whether similar changes can be induced by adaptation to CO exposure remains to be determined.

Only one investigator has reported that adaptation to CO can be demonstrated experimentally in humans. Killick[86] exposed herself to 220 to 520 mg/m^3 (190 to 450 ppm) CO in air for periods of 5 to 7 hours at approximately weekly intervals for a period of 6 months. The resulting COHb level at equilibrium ranged from 16.5 percent at 255 mg/m^3 (220 ppm) CO to 39.5 percent at 460 mg/m^3 (400 ppm) CO. COHb was determined with a reversion spectroscope; this method permits subjective errors, and the COHb levels reported in this paper may be inaccurate. CO was measured by the iodine pentoxide method. Killick considered adaptation to have taken place when (1) there was a diminution in symptoms with repeated exposure to the same concentration of CO, and (2) a discrepancy between the observed COHb at the end of an exposure was less than the COHb obtained *in vitro* when the subject's blood was equilibrated with a mixture containing oxygen and CO at the same partial pressure as in the alveolar air. The conclusions of this study are open to question, since a basis for determining the development of adaptation was a difference between observed and calculated COHb levels. The methods used for calculation resulted in a calculated arterial P_{O_2} as much as 100 mm Hg above alveolar P_{O_2}. The irregular pattern of exposure, possible erroneous calculations, and subjective methods for COHb determination render limited value to this study. In contrast to Wilks' study in dogs, however, Killick found no change in the RBC count or in the blood volume.

In summary, it can only be stated that the available data concerning physiologic adaptation of humans to CO are inconclusive. It is expected that some adaptation will take place, but the mechanism is unclear.

J. ENDOGENOUS FORMATION OF CARBON MONOXIDE

The first claims that CO could be formed within the mammalian body were reported by French investigators in the period 1898 to 1925,[87-91] but an exogenous source of the CO could not be ruled out. In 1945, Roughton and Root[92] demonstrated that there was a small, but measurable, amount of CO in normal human blood. In 1949, Sjöstrand[93] observed that the expired air of human subjects who were not exposed to exogenous CO contained consistently more CO than the inspired air, suggesting that CO was being produced in the body. Sjöstrand's findings were confirmed by Coburn[94] et al.; with the use of a sensitive anlytical method for blood CO, these workers were able to measure directly the rate of CO formation by using a rebreathing system. The average rate of CO production in man was found by Coburn et al. to be 0.42 ± 0.07 ml per hour; this is slightly lower than Sjöstrand's value of 0.5 to 1.0 ml per hour in the normal adult female.

Utilizing a rebreathing system and the Haldane equation, Sjöstrand estimated an indirect value for COHb from the rebreathing gas samples at the end of the rebreathing period.[21] Both Sjöstrand[95] and Engstedt[96] have noted that the COHb level thus calculated is positively correlated with the presence of hemolytic disease or other states associated with increased hemoglobin breakdown, such as extensive trauma or mismatched transfusions.[97,98] These findings have been more precisely confirmed by Coburn[94,99] et al. with their improved analytical techniques.

Sjostrand[100] has also demonstrated that solutions of hemoglobin and myoglobin liberate CO upon standing, and that maximal production of CO from such solutions corresponds to the CO-binding capacity of the initial solution. Injections of hemolyzed blood and hemoglobin solutions into humans, dogs, and rabbits have been observed to cause an increased endogenous production of CO.[101,102] By injecting damaged erythrocytes, Coburn[99] et al. have demonstrated a molar ratio between the amount of heme destroyed and the amount of increase in CO formation. The increase in CO formation occurs simultaneously with rising levels of serum bilirubin, a metabolic product of hemoglobin.

The experimental data indicate that endogenous CO is a by-product of heme catabolism. *In vivo,* the end products of hemoglobin catabolism are the bile pigments, which arise specifically from the heme group of the hemoglobin. Heme, which is a cyclic tetrapyrrole, loses its α-methene-bridge carbon atom to form bilirubin, which is linear tetrapyrrole. Libowitzky and Fischer[103] have been unable to recover this missing one-carbon fragment *in vitro* as either formic acid or formaldehyde. Sjöstrand[100-102] has suggested that the missing carbon atom is incompletely oxidized, forming CO which is then excreted in the expired air. Ludwig[104] et al. have confirmed this suggestion by using ^{14}C-labeled heme.

Other heme-containing proteins are also likely sources of endogenous CO, provided that the initial steps of their catabolism are similar to those of hemoglobin. It is known that approximately 10 to 15 percent of the total bile pigment production comes from sources other than circulating red cell hemoglobin. These sources[105] may be:

1. Myoglobin heme catabolism.
2. Catabolism of heme-containing enzymes (cytochromes, catalases, etc.).
3. Excess production of heme in marrow and other sites.
4. Production of bilirubin through anabolic pathways.
5. Early death of red blood cells within the marrow or shortly after their release (ineffective erythropoiesis).
6. A scarf of hemoglobin around the extruded nucleus of the normoblast.

In their radioactive tracer studies, White et al. have demonstrated that labeled CO was produced within the first few days following injection of glycine-2-^{14}C. This radioactive amino acid specifically labels that α-methene-bridge carbon atom of heme. The amount of labeled CO recovered was of the correct order of magnitude to account for the excess CO.[106] Similar results have been reported in studies of heme catabolism in rodents.[107] In addition, White[108] et al. have demonstrated the production of CO from liver slices *in vitro,* with the simultaneous production of bilirubin. This has confirmed earlier studies[109,110] demonstrating that nonhemoglobin hemes in the liver are important sources of bile pigment. Schwartz[111] et al., using hypertransfused mice in which erythropoiesis was nearly 100 percent suppressed, have estimated that about 40 percent of the early appearing bile pigment (and CO) was due to catabolism of nonhemoglobin hemes. Recently, direct evidence of increased CO production in states associated with increased ineffective erythropoiesis has been obtained.[112]

An appreciation of the importance of endogenously produced CO in clinical and experimental conditions is developing. It has been noted that patients presumably not exposed to CO do, when undergoing anesthesia, produce CO levels within rebreathing anesthesia apparatus; these CO concentrations often exceed 58 to 115 mg/m^3 (50 to 100 ppm).[113] This concentration exceeds the maximum allowable levels for industrial workers who are exposed to CO for 8 hours. It has been suggested that these closed rebreathing systems be opened and flushed periodically during the operative procedure in order to remove the excess CO. Some of this increase in CO during anesthesia may be due to the increased oxygen tension of inspired air, which, according to the Haldane equation,[114,115] will promote the dissociation of COHb. Increased COHb levels are also seen in newborn infants,[114,115] because of both normal and abnormal hemolysis. The endogenous production of CO in the newborn leads to increased COHb levels (up to 12 percent) and results in relation impairment of oxygen-transport function.

It has long been known that CO arising from internal combustion engines, tobacco smoke, and other conventional sources in submarines is an important cause of atmospheric pollution in the crew's quarters. In other closed systems containing men or animals, the puzzling production of CO has been noted. Toxic or fatal CO levels have even occurred in some animal experiments when the contaminant was not specifically removed. It is implied that the crew members (or the experimental animals) themselves are an important source of CO pollution in closed systems. Greater attention is now being focused on the endogenous production of CO in closed systems that are being evaluated for use in space flights and undersea exploration.

It is conceivable that animal-plant cycles proposed for long space flights as oxygen producers and waste-product removers may themselves turn out to be an additional source of CO. This could result from the decomposition of chlorophyll - the green pigment of plants - which contains a cyclic tetrapyrrole structure similar to heme. Mature leaves have been shown to produce large quantities of CO, presumably from degradation of chlorophyll.[116]

There is the possibility that a CO cycle exists in nature, since it has been demonstrated that many animal and plant species produce this compound.[116-120] Carbon monoxide can also be utilized for metabolic purposes in certain bacteria[121] and plants,[122] and may even be oxidized to CO_2 at slow rates in animals[123] and in man.[66] A more detailed discussion of possible biological sources of CO appears in Chapter 2.

K. SUMMARY

Carbon monoxide is absorbed exclusively via the lungs, and most of its toxic properties are a result of its reaction with hemoproteins. The primary effect of CO is mediated by its reaction with hemoglobin to form carboxyhemoglobin (COHb), thus reducing the oxygen-carrying capacity of the blood and accounting for about 80 percent of an inhaled dose of CO. The affinity of hemoglobin for CO is over 200 times that for oxygen, indicating that COHb is more stable than oxyhemoglobin (O_2Hb). The presence of COHb also shifts the O_2Hb dissociation curve to the left, implying that, at the tissue level of the circulation, less oxygen is available to the cells because of the decrease in oxygen tension (P_{O_2}). About 20 percent of a given dose of CO passes from the intravascular to the extravascular pool, reacting primarily with myoglobin to form carboxymyoglobin (COMb). About 1 percent or less reacts with the heme-containing cytochromes, and at CO concentrations commonly encountered in community air pollution, this reaction is unlikely to be of any physiological significance.

The most accurate analysis of relatively low blood COHb concentrations results from the spectrophotometric determination (NDIR method) of the CO liberated from the blood when the hemoglobin is destroyed. The necessary equipment is quite costly, a tedious procedure is involved, and relatively large blood samples are required. Several other good methods exist for the determination of low blood CO levels. The normal "background" concentration of blood COHb is about 0.5 percent, and this is attributed to endogenous sources such as heme catabolism. The body uptake of exogenous CO increases with the concentration, length of exposure, and ventilatory rate. When the concentration remains constant, a state of equilibrium is reached in which the partial pressure of CO (P_{CO}) in the pulmonary capillary blood is almost equal to that in the alveolar and ambient air. The rate of uptake of CO is fairly constant with respect to blood COHb until about one-third of the equilibrium value is reached, and then this uptake proceeds at a slower and slower pace. Human exposure to 35 mg/m^3 (30 ppm) CO has shown that about 80 percent of the equilibrium value of 5 percent COHb is reached within 4 hours, and the remaining 20 percent is achieved slowly over the next 8 hours. It is estimated that exposure of a previously nonexposed individual to 23 mg/m^3 (20 ppm) CO for about 8 or more hours would result in a blood COHb level of about 3.7 percent; exposure to 12 mg/m^3 (10 ppm) for a similar period of time would probably result in a blood COHb level of about 2.1 percent.

The observed toxic effects of CO in both animals and humans reflect the impairment of the oxygen transport system. The data on experimental exposures of animals and humans are shown in tables 8-15 and 8-16.

Long-term exposure of animals to CO may produce morphological changes in the heart and brain. Dogs exposed intermittently or continuously to 58 mg/m^3 (50 ppm) for 6 weeks have developed abnormal EKG's after the third week. At autopsy, these same dogs have shown mobilization of glia and dilatation of the lateral ventricles of the brain. In another study, continuous exposure of dogs to 58 mg/m^3 for 3 months has failed to show such changes, but significant increases in hemoglobin levels, hematocrits, and RBC counts were observed. Continuous and intermittent exposure of dogs to 115 mg/m^3 (100 ppm) for 6 weeks has produced a dilatation of the chambers of the right heart and, occasionally, of the left heart, and some degeneration of heart muscle has also been noted. Dogs exposed to 115 mg/m^3 for 5¾ hours a day, 6 days a week for 11 weeks have developed a consistent disturbance of the postural reflexes and of gait, although no changes in the electroencephalogram (EEG) or the peripheral nerves were reported. At autopsy, there was some indication of cortical damage.

The effects of CO on the hematological system of animals suggest the possibility of adaptation to CO. Cholesterol-fed rabbits that were adapted (acclimatized) by exposure to 195 mg/m^3 (170 ppm) CO for 8 weeks have shown an increase in the hemoglobin level during the first 5 weeks of exposure; the level stabilized during the following 3 weeks. When the CO concentration was increased to 405 mg/m^3 (350 ppm), a further increase in hemoglobin was observed.

Short-term exposure of animals to low levels of CO have produced effects on the central nervous system. Rats exposed to 58 mg/m^3 (50 ppm) for 1 hour have developed alterations in the electroencephalogram (EEG), which have increased in severity with longer periods of exposure. These changes have returned to normal 48 hours after the end of the exposure. After exposure to 58 mg/m^3 for 48 minutes, rats have developed an impairment in time discrimination. Short-term exposure to higher CO concentrations has produced similar effects, but with increased severity.

No long-term human studies on experimental CO exposures have been reported, although there are data on occupational exposures. Brief exposures to high levels of CO have produced effects on the central nervous, vascular, and respiratory systems. Central nervous system effects appear to occur at COHb levels above 2 percent. Exposure of nonsmokers to 58 to 290 mg/m^3 (50 to 250 ppm) CO for up to 2 hours has produced a significant impairment in time discrimination, statistically significant at about 58 mg/m^3 for 90 minutes (approximately 2.5 percent

Table 8–15. SUMMARY OF EFFECTS OF CARBON MONOXIDE IN ANIMALS

Species	CO level	Length of exposure	COHb, %	Effect	Reference
Dogs	58 mg/m^3 (50 ppm)	6 hrs/day, 5 days/wk, for 6 wk 24 hr/day, 7 days/wk, for 6 wk	2.6 to 5.5	Brain: Mobilization of glia and dilatation of lateral ventricles. Necrosis and dilineation absent. Heart: 10/15 developed EKG changes in third week.	Lindenberg[38] et al.
Rats Rabbits Dogs	58 mg/m^3 (50 ppm)	24 hr/day, 7 days/wk, for 3 mo	Rats 1.8 Rabbits 3.2 Dogs 7.3	Dogs: No changes in EKG's and pulse rates. No histologic difference between exposed and control animals. Significant increases in hemoglobin levels, hematocrits, and RBC counts.	Musselman[55] et al.
Rats	58 mg/m^3 (50 ppm)	24 hr/day, 7 days/wk, for 3 mo		EKG changes in the first 2 weeks returning to normal in third week. Slight increase in hemoglobin levels, hematocrits, and RBC counts.	Roussel[56] et al.
Rats	58 mg/m^3 (50 ppm)	1 hr 1 to 5 hr/day for 4 days		Changes in EEG increasing in severity with length of exposure. Progressive deterioration in EEG returning to normal 48 hours after end of exposure.	Xintaras[40] et al.
Dogs	115 mg/m^3 (100 ppm)	6 hr/day, 5 days/wk, for 6 wk 24 hr/day, 7 days/wk, for 6 wk	7 to 12	Brain: Mobilization of glia and dilatation of lateral ventricles. Necrosis and demyelination absent. Heart: 8/8 developed abnormal EKG's after about 2 weeks. Autopsy: dilatation of right heart and occasionally of left heart; some degeneration of heart muscle.	Lindenberg[38] et al.
Dogs	115 mg/m^3 (100 ppm)	5-3/4 hr/day, 6 days/wk, for 11 wk	up to 21	Brain: No changes in EEG or in peripheral nerves. Consistent disturbance of postural reflexes and gait. Autopsy: 6/6 showed some indication of cortical damage. Heart: 1/4 had inverted T-wave after second week 2/4 had inverted T-wave by tenth week Autopsy: 4/4 showed degenerative changes in muscle fibers.	Lewey and Drabkin[37]

Table 8-15 (continued). SUMMARY OF EFFECTS OF CARBON MONOXIDE IN ANIMALS

Species	CO level	Length of exposure	COHb, %	Effect	Reference
Rats	115 to 11,500 mg/m^3 (100 to 10,000 ppm)	up to 48 min.	n.a.	Impairment in time discrimination.	Beard and Wertheim[39]
Rabbits	195 mg/m^3 (170 ppm)	8 weeks	19.7 at end of first week	Decrease in % COHb from 19.7 to 15.1. Increase in hemoglobin level in first five weeks followed by stabilization. Exposure to 400 mg/m^3 (350 ppm) caused further increase in Hb. Rats were cholesterol fed. Increased total cholesterol in aortic tissue in rabbits exposed to CO.	Astrup[57,75] et al.
Dogs	920 to 1150 mg/m^3 (800 to 1000 ppm)	6 to 8 hr/day, 7 days/wk, for 36 wks		Increased RBC counts, hemoglobin, and blood volume. Challenge with 575 mg/m^3 (500 ppm) in these dogs produced the same % COHb as in non-acclimatized controls.	Wilks[85] et al.
Dogs	>1,150 mg/m^3 (1,000 ppm)	n.a.	3 to 40	Prominent EKG changes. High mortality rate. Alterations in cerebral and myocardial histology.	Preziosi[58]
Dogs	115 mg/m^3 (100 ppm)	6 wk, continuous and intermittent	7 to 12	EKG changes, more marked with continuous than intermittent exposure. Dilatation of right cardiac chamber. Dilatation of lateral ventricles of the brain.	Preziosi[58]
	58 mg/m^3 (50 ppm)	6 wks, continuous and intermittent	2.6 to 5.5	Same changes as noted with exposure to 115 mg/m^3, except EKG changes were not as prominent.	
Mice	58 mg/m^3 (50 ppm)	3 mo to 2 yr	n.a.	No changes noted in fertility, fetal survival, body growth, food intake, weight and water content of various organs, EKG, or blood chemistries.	Stupfel[41]
Monkeys	55 mg/m^3 (48 ppm)	n.a.	3.7 to 4.7	No decrement in performance, even at simulated altitude of 27,000 feet.	Back and Dominguez[42]

Table 8–16. SUMMARY OF EFFECTS OF CARBON MONOXIDE IN HUMANS

No. subjects	CO level	Length of exposure	COHb, %	Effect	Reference
7	115 to 23,000 mg/m^3 (100 to 20,000 ppm)	Up to 5 hr	Up to 35.0	1. Uptake of CO increases with (a) concentration of CO, (b) length of exposure, (c) ventilation rate. 2. Rate of uptake of CO as measured by increase in blood % COHb is constant up to 1/3 of equilibrium COHb. 3. Rate of uptake decreases with increased P_{O_2} and apparently increases with decreased P_{O_2} due to hyperventilation. When the latter is corrected for, rate of uptake is unaltered.	Forbes[29] et al.
10	35 mg/m^3 (30 ppm)	24 hr	5	Approximate equilibrium value of COHb reached by 12 hours; 60% of equilibrium value reached in 2 hours, 80% in 4 hours, and the remainder over 8 hours.	Smith[33]
4	100% (100 to 300 ml)	10 to 15 min	Up to 20	Impairment of visual function detectable at approximately 4.5% COHb and increases with increase in COHb. Recovery lags behind excretion of CO. Latter depends on composition of gas during post-exposure period. Experiments at simulated altitudes gave a similar pattern of results. Data given for one subject only.	Halperin[52] et al.
1	n.a. (1 cigarette)	n.a.	2	Impairment of visual function	MacFarland[50] et al.
1	n.a. (3 cigarettes)	n.a.	4	Impairment of visual function similar to that produced by an altitude of 8,000 ft.	
49	n.a.	n.a.	Up to 20.4	Impairment in response to certain psychomotor tests, detectable at 5% COHb. No effect on pulse, respiratory rate, blood pressure, neurological reflexes, muscle persistence, and static steadiness test.	Schulte[44]
18	58 to 230 mg/m^3 (50 to 250 ppm)	Up to 2 hr	2.5	Significant impairment in time-interval discrimination after exposure to 58 mg/m^3 (50 ppm) for 90 minutes.	Beard and Wertheim[39]

Table 8-16 (continued). SUMMARY OF EFFECTS OF CARBON MONOXIDE IN HUMANS

No. subjects	CO level	Length of exposure	COHb, %	Effect	Reference
4	58 to 230 mg/m^3 (50 to 250 ppm)	Up to 2 hr	3	Consistent impairment in 3 of 4 parameters of visual function after exposure to 58 mg/m^3 for 50 minutes	Beard and Grandstaff[51]
18	29 to 1,150 mg/m^3 (25 to 1,000)	Up to 16 hr	Up to 31.8	No impairment of time estimation. No change in blood chemistries.	Stewart[46] et al.
	Up to 115 mg/m^3 (100 ppm)	8 hr	11 to 13	No impairment in psychomotor test performance.	
5	n.a.	Up to 2 min	Above 5	Decreased P_{aO_2} and P_{vO_2}	Ayres[62] et al.
26	n.a.	Up to 2 min	Above 5 (average 8.96).	Increased oxygen extraction in the presence of COHb.	Ayres[63] et al.
11	n.a.	Up to 2 min	Above 5 (average 8.5 to 9).	Increased lactate production in patients with coronary heart disease; in patients with non-coronary heart disease, increased coronary blood flow, and fall in mixed venous and coronary sinus P_{O_2}.	

COHb). At blood COHb levels of about 3 percent (estimated by expired air analysis after exposure to 58 mg/m^3 of CO for 50 minutes), significant changes in relative brightness threshold and visual acuity have been observed. Impairment in the performance of certain psychomotor tests has occurred at about 5 percent COHb. Exposure of four subjects to 100 to 300 ml of pure CO for several minutes has produced an impairment in visual function, which was significant when the blood COHb level in one subject reached about 4.5 percent.

Changes in the cardiovascular system of humans have been measured at COHb levels greater than those associated with central nervous system effects. Exposure to CO affects oxidative metabolism of both systemic and myocardial circulatory beds. Blood COHb levels above 5 percent in five subjects have produced a mean decrease of 13.3 percent in mixed venous oxygen tension and 7.3 percent in arterial oxygen tension. In 26 subjects whose mean COHb was 8.9 percent, there was a mean decrease in the venous P_{O_2} that could be correlated with an increase in COHb. There were also associated increases in oxygen extraction ratios, ventilation, and cardiac output.

Myocardial metabolic studies have demonstrated that concentrations of CO sufficient to produce significant increases in COHb may produce a severe burden in subjects who already have increased demands on their oxygen supply, such as persons with coronary artery disease. Eleven cardiac patients, four of whom had coronary artery disease, were exposed to CO that produced a mean COHb level of almost 9 percent, with several patients having blood COHb levels in the range of 5.5 to 6.5 percent. Patients with noncoronary heart disease showed a compensatory increase in coronary blood flow in response to the increased myocardial oxygen needs; this response did not occur in the four patients with coronary heart disease. In addition, the inadequate oxygen supply to the myocardium was reflected in the lactate extraction ratio, which changed to production in these four patients. It thus appears that persons with certain forms of heart disease may be particularly susceptible to exposures of CO that could lead to blood COHb levels in excess of 5 percent.

The effects of CO are especially important at altitude because of the lowered P_{O_2}. Both physiological and psychomotor tests have been employed to demonstrate these effects. As indicated by the increase in exercise pulse rate, each increase of blood COHb of 1 percent, up to 13 percent, has been shown to be equal in effect to about 335 feet of altitude, applied over the altitude range of from 7,000 to 10,000 feet. Impairment of visual threshold perception in a single subject at 7,000 feet was equivalent to that produced by 5 percent COHb at sea level. In five subjects, a COHb level of 8 to 10 percent has produced a mean impairment in flicker fusion frequency (FFF) that was equivalent to lowering the altitude tolerance 4,000 feet (from about 10,000 to 6,000 feet).

In many of the human studies, the brief exposures to very high levels of CO make it difficult to relate the observed effects to equilibrium COHb levels. For long-term exposure to CO, certain effects such as increased hematocrits, hemoglobin levels, and blood volume may be present, but the available data are inadequate to draw firm conclusions concerning the significance of all of these changes.

In summary, appraisal of short-term experimental exposures of humans to CO shows the following results in terms of the blood COHb levels observed:

1. No human health effects have been demonstrated nor have they been observed for COHb levels of 0 to 1 percent, since endogenous CO production makes this a physiological range.
2. The following effects on the central nervous system have been observed at 2 to 5 percent COHb:
    a. At an estimated level of about 2.5 percent COHb in nonsmokers (based on exposure to 58 mg/m^3 CO for 90

minutes), an impairment in time-interval discrimination has been demonstrated.

b. At COHb levels of about 3 percent (based on exposure to 58 mg/m^3 for 50 minutes), changes in visual acuity and relative brightness threshold have been documented.

c. At about 5 percent COHb, an impairment in the performance of certain other psychomotor tests, and an impairment in visual discrimination, have been demonstrated.

3. The following cardiovascular changes have been observed at COHb levels above 5 percent:

   Increased cardiac output, systemic arterio-venous oxygen-content difference, systemic oxygen extraction ratios, myocardial arterio-venous oxygen-content difference, and coronary blood flow in patients without coronary heart disease. In patients with coronary heart disease, lactate extraction changes to production and the compensatory *increase in coronary* blood flow is absent.

The concentrations of CO necessary to result in such blood COHb levels are a function of ventilatory rate and length of exposure.

Long-term experimental exposure of humans to CO may produce certain adaptive effects such as increased hemoglobin levels and hematocrits, but the available data are inadequate to draw firm conclusions. Such effects have been observed in animals. There is a definite need to further evaluate the effect of cigarette smoking on the central nervous system and cardiovascular system, as well as the possible "adaptation" of the cigarette smoker to CO.

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CHAPTER 9.

EPIDEMIOLOGIC APPRAISAL OF CARBON MONOXIDE

A. INTRODUCTION

Studies to determine the effects of CO upon health have usually involved short-term high-concentration exposure to CO; therefore, the observed clinical effects are often attributable to hypoxia. Many of these effects are considered to be reversible as CO is eliminated from the body.[1,2] A number of recent clinical and laboratory studies have resulted in the concern that subtle cardiovascular and central nervous system effects may be associated with elevated CO levels in the atmosphere.

Epidemiologic studies, as distinguished from toxicologic or experimental studies, deal with the effects of pollution from the ambient air on groups of people living or working in a community or area. In such studies health effects are examined as they occur naturally, rather than in a laboratory; but this type of study also has the disadvantage that all the factors of possible importance cannot be controlled. Nevertheless, the preparation of air quality criteria and air quality standards usually relies on epidemiologic studies because of the limitations inherent in most laboratory studies.

In air pollution epidemiology, gross mortality data have been an insensitive way of measuring health effects. Further, there is often inappropriate designation of cause of death, variation in certification of cause of death, and usually a lack of autopsy data. Systematic study of morbidity associated with exposure to CO is handicapped by this lack of available indices of health effects.

Hospital admissions data are one form of useful information; but problems due to variability in availability of beds, day-of-week biases, changing medical staff, overtime, and altered criteria for admission make this information susceptible to misinterpretation. Some of these problems have been dealt with by Sterling et al. in a study utilizing Blue Cross hospital admission data as an index of morbidity.[3,4]

The problems of associating monitoring station data with the actual impact on the individual who is exposed to a number of environments during the course of a day has been dealt with by Goldsmith et al.[5] Because of the relative ease in determining carboxyhemoglobin (COHb) levels by the analysis of expired air, the potential for using each individual as his own monitoring system should be considered in many cases.[6] In several occupational studies COHb levels have been measured in individuals exposed to high concentration of CO and attempts have been made to relate COHb levels to health effects. These studies are discussed in the following sections.

B. SOURCES AND MAGNITUDE OF EXPOSURE TO CARBON MONOXIDE

The numerous sources of CO and their relative contribution to body COHb levels are just beginning to be assessed. In addition to the CO encountered in community air, man is personally exposed to individual sources such as cigarette smoke, household heaters, cooking fumes, and occupational pollution. Detecting and estimating the contribution of community air pollution in the presence of multiple exposures poses a complex problem. Fortunately, it is easy to estimate the amount of CO in the body by expired air analysis after 20-second breathholding.[7-9] Limitations in the application of this method to nonsmokers are discussed in Chapter 8, Section C.3.

1. Community and Residential Exposures

Because of the large number of motor vehicles, CO is produced in sufficiently large quantities in certain cities that it can no longer be considered a problem in only the immediate vicinity of traffic; it may now be found throughout entire communities.[10,11] A quantitative discussion on the extent of this problem is given in Chapter 4, Section B.

Haagen-Smit has measured the CO levels to which the commuter is exposed in Los Angeles city traffic.[12] He found that the average concentration was 43 mg/m^3 (37 ppm) CO and that this level increased to 62 mg/m^3 (54 ppm) in slow and heavy traffic.

Goldsmith et al. have reported on the increase in COHb in two pairs of subjects, - a smoker and a nonsmoker in each pair - exposed together to Los Angeles conditions.[5,8] Some results of this work are shown in Figures 9–1 and 9–2.

A theoretical approach has been postulated to estimate effects of population exposure to CO by inference from an exposure pattern and indirect measurement of the mean COHb

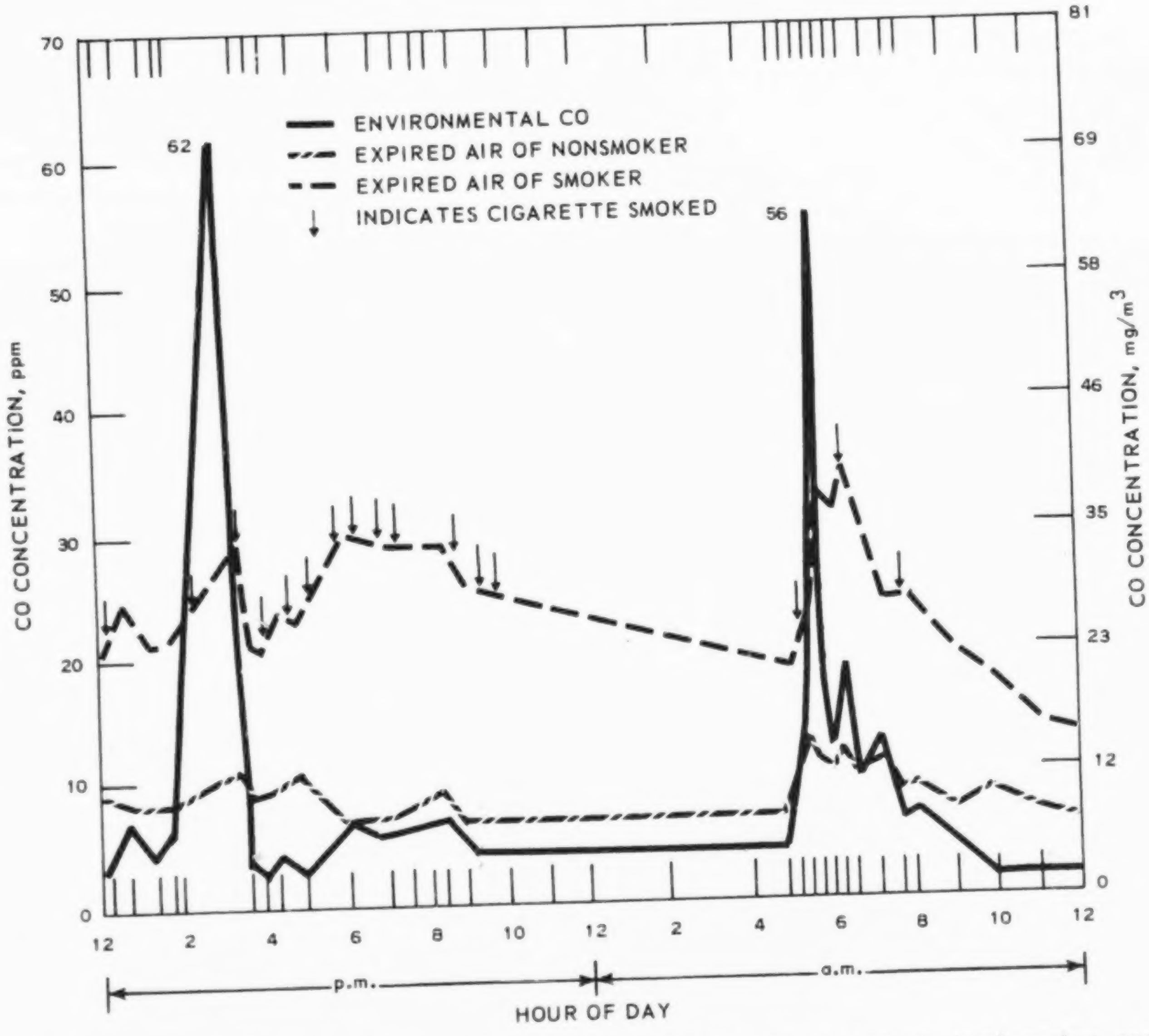

Figure 9-1. Carbon monoxide levels of environmental air and of expired air of smoker and nonsmoker, Los Angeles and Pasadena, August 1962.[5]

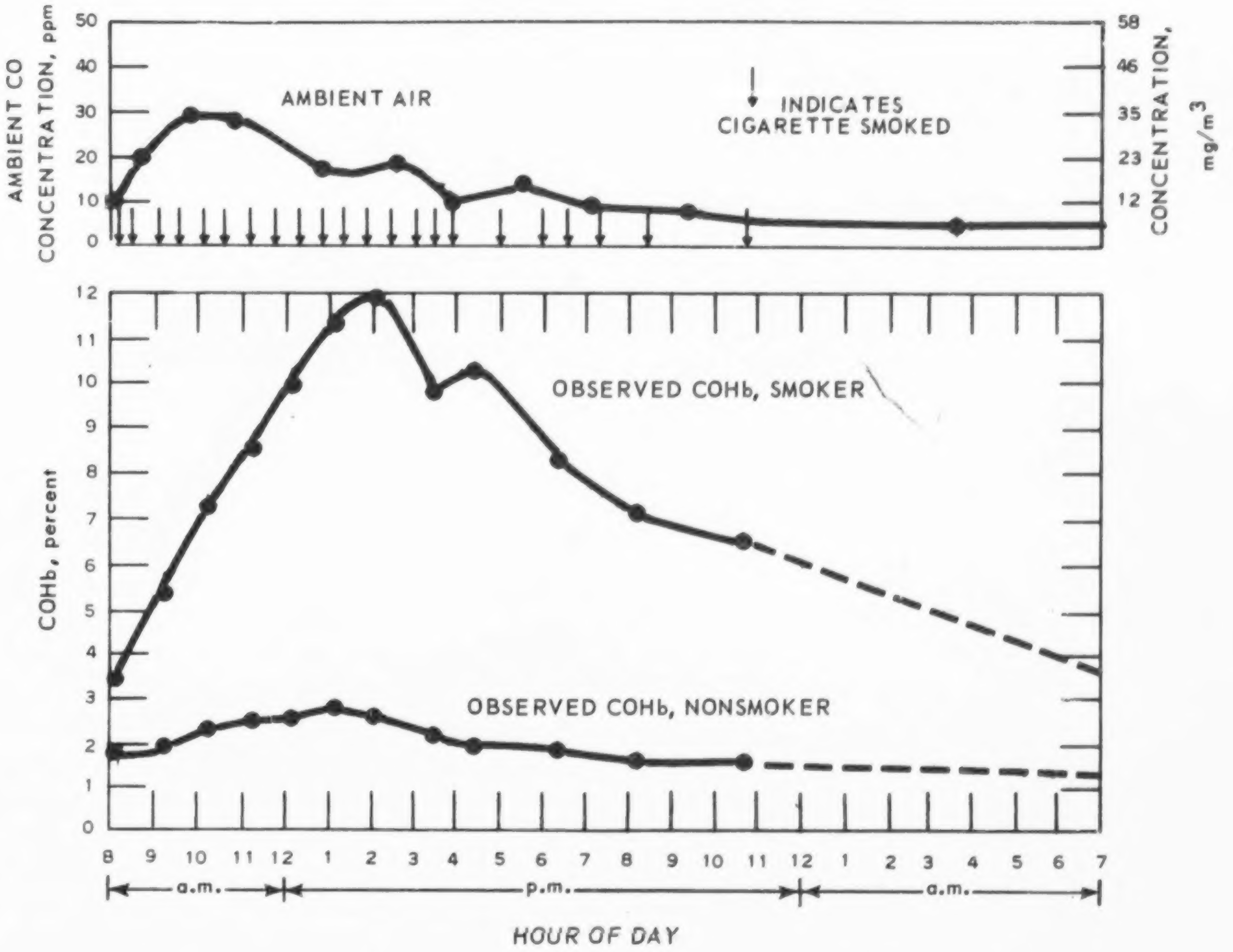

Figure 9-2. Carbon monoxide levels of environmental air and COHb levels of smoker and nonsmoker, Los Angeles County, 1963.[8]

levels in the population. The application of such a procedure would be more valid than current methods of environmental surveillance.

A recent review describes several household sources of CO.[13] In addition it has also been shown that open fires and charcoal braziers produce a substantial amount of CO.[14] A field study in New Guinea also indicates that high levels of CO may be present in native huts when cooking is done.[15] Some of the seasonal variation reported for COHb concentrations in individuals may be attributable to household heating. A further discussion of levels of CO measured in households appears in Chapter 6, Section D.

Community CO levels have been monitored in a variety of areas to determine the distribution and magnitude of exposure. Very little attention, however, has been directed toward the influence of community exposure upon household CO levels.

2. Occupational Exposures

Most epidemiologic studies of the effects of CO on human health have dealt with occupationally exposed groups. These studies cannot be extrapolated quantitatively to the general population because persons with severe anemia, cardiovascular insufficiency, or other debilitating conditions are unlikely to be working in places like traffic tunnels, steel mills, or parking garages. In addition, people occupationally exposed to CO may simultaneously be exposed to a number of other environmental sources of CO, and the contribution of each possible source may be difficult to isolate. The effects usually observed in occupational studies of CO are increased levels of COHb and the disputed "chronic carbon monoxide poisoning syndrome,"[16,17] which consists of recurrent symptoms such as headache, dizziness, exertional dyspnea, diarrhea, urinary frequency, sweating, thirst, weight loss, loss of libido, and insomnia.

Grut studied drivers of vehicles propelled with "producer gas" in Copenhagen during World War II; he indicated that 46 percent of 721 drivers had chronic CO poisoning, characterized by fatigue, headache, irritability, dizziness, and disturbed sleep.[16]

Lindgren examined two similar groups of workmen, one of which was occupationally exposed to CO.[17] The exposed group, with significantly higher COHb levels, included 970 subjects; the control group included 432 subjects. He found no higher frequency of symptoms and signs typical of chronic CO poisoning in the exposed group than in the control group. He also found no differences in the frequency of illness between the two groups, based on national health insurance records over a period of 10 years.

An important study of occupational exposure to CO was conducted among employees of New York's Holland Tunnel.[18,19] The average exposure through all parts of the tunnel throughout the day was estimated to be 80 mg/m^3 (70 ppm), with peak concentrations rarely higher than 230 mg/m^3 (200 ppm). The levels of CO found in the blood of traffic officers stationed in the tunnel for a 2-hour period were within the range usually observed in cigarette smokers with no occupational exposure to CO. In addition, the amounts of CO absorbed during tunnel duty appeared to add to amounts acquired from cigarette smoking. No complaints attributable to CO exposure were noted. Hemoglobin determinations were reported as normal for all exposed individuals. Urinalysis did not reveal abnormalities of glucose or albumin when compared with other populations.

Hofreuter et al. studied 68 employees of a vehicle inspection center where hourly CO concentrations averaged 58 mg/m^3 (50 ppm), with these measurements ranging from 12 to 173 mg/m^3 (10 to 150 ppm).[20] The average blood COHb level for this exposed group was 3.74 percent; this was significantly higher ($p<0.01$) than the average of 2.67 percent COHb found in a control group. Average hemoglobin levels were also significantly higher in the exposed group. The high average COHb level in the control group is attributed to the majority of subjects in each group being smokers.

Ramsey studied 38 parking garage employees whose occupational exposure to CO averaged 68 mg/m^3 (59 ppm) during the work day.[21] COHb levels in these individuals were significantly different from those in a control group not exposed to motor vehicle exhaust. Their hemoglobin levels were also significantly higher than those of control subjects. Ramsey felt that occupational exposure appeared more important than smoking in determining COHb level in this group (See Table 9-1).

de Bruin measured COHb levels of policemen and drivers in Rotterdam and Amsterdam.[22] Blood samples obtained before and after work showed increased COHb in those occupationally exposed. A control group showed no such increase.

Clayton et al. found increases in COHb levels in smoking (3.1 to 3.9 percent COHb)

Table 9-1. COHb LEVELS OF SMOKERS AND NONSMOKERS IN EXPOSED AND CONTROL GROUPS[22]

Group		COHb, %			
		a.m.		p.m.	
		Mean	S D	Mean	S D
Exposed (parking garage)					
Nonsmokers	14	1.5	±0.83	7.3	±3.46
Smokers	24	2.9	±1.88	9.3	±3.16
Controls					
Nonsmokers	10	...	....	0.81	±0.54
Smokers	17	...	....	3.9	±1.48

and nonsmoking (0.8 to 1.2 percent COHb) subjects travelling in a police scout car for 8 hours in traffic; the average CO level measured during this period was 20 mg/m^3 (17 ppm) although a peak of 138 mg/m^3 (120 ppm) was recorded.[23] After also studying the COHb levels of 237 individuals involved in traffic accidents, these authors concluded that the CO level in the Detroit urban area does not appear to be related to impaired driving ability. It is interesting to note that the information presented in Table 9-2 and Figure 9-3 shows that drivers involved in accidents had higher COHb levels than did pedestrians, though the differences are not statistically significant. No attempt was made to relate accident rate to ambient CO level in this study. The implications of the possible relationship between ambient levels of CO, blood COHb levels, and the occurrence of motor vehicle accidents suggest that this is an important area for future research.

Table 9-2. FREQUENCY DISTRIBUTION OF CO BLOOD ANALYSES OF INDIVIDUALS INVOLVED IN TRAFFIC ACCIDENTS[23]

COHb, %	Total number of analyses (cumulative percent in parentheses)	Status of individuals involved[a]			
		Drivers	Pedestrians	Passengers	Status unknown
1.0	73 (32.2)	27	30	5	11
1.0- 1.9	45 (52.0)	21	17	1	6
2.0- 2.9	30 (65.2)	14	11	1	4
3.0- 3.9	14 (71.4)	6	6	-	2
4.0- 4.9	25 (82.4)	12	6	3	4
5.0- 5.9	14 (88.5)	6	7	-	1
6.0- 6.9	10 (93.0)	3	4	1	2
7.0- 7.9	7 (96.0)	5	2	-	-
8.0- 8.9	4 (98.0)	3	1	-	-
9.0- 9.9	2 (98.7)	2	-	-	-
10.0-10.9	1 (99.1)	-	-	-	1
11.0-11.9	1 (99.6)	1	-	-	-
31.5	1 (100)	-	-	-	1
Clotted	7	2	3	1	1
Broken	3	1	2	-	-
Totals	237	103	89	12	33

[a] The difference in COHb between drivers and pedestrians is not statistically significant.

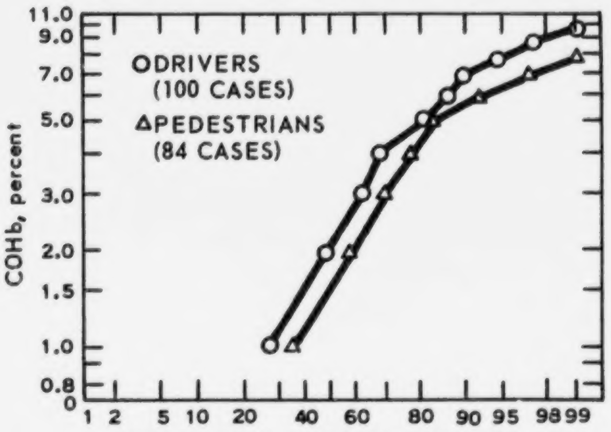

Figure 9-3. Distribution of COHb among individuals involved in traffic accidents.[23]

Chovin has studied 331 traffic policemen in Paris. Determinations of COHb were made before and after a 5-hour work period, with average CO exposures of 12 to 14 mg/m^3 (10 to 12 ppm).[24] Cigarette smokers who started work with relatively high COHb levels but did not smoke while at work tended to excrete CO, whereas similar smokers who started work with low levels tended to have an increase in COHb. Those who had COHb levels of 3 to 8 percent at the beginning of the work shift showed very little change (See Figure

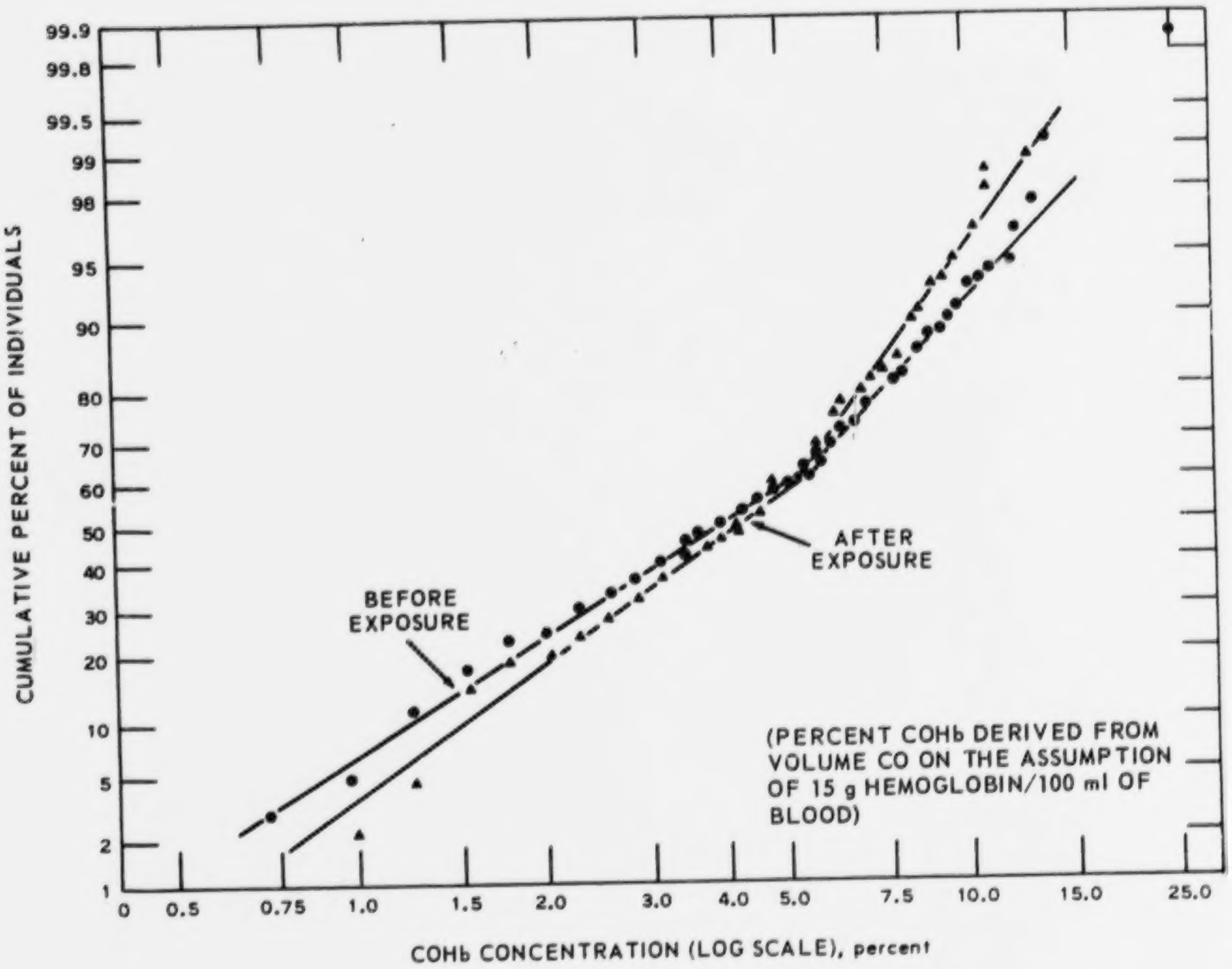

Figure 9-4. COHb levels of policemen who smoke before and 5 hours after exposure to between 12 and 23 mg/m^3 (10 and 12 ppm) CO, Paris, 1963.[24]

9-4). Nonsmokers had an increase in COHb that was related to the ambient exposure at the intersection where they were directing traffic (See Figure 9-5).

Chovin derived the equation:

$$I_{CO} = 0.024C-0.07$$

to depict the manner in which blood CO equilibrium is approached after a person is exposed to traffic for 5 hours. I_{CO} is the increase in blood CO (in cc of CO/100 cc blood), and C is the average ambient CO concentration (ppm). This equation can be expressed in terms of change in percent COHb as follows:

$$\Delta \% \text{COHb} = 0.096C - 0.28$$

Thus, for example, an average 5-hour exposure to 22 mg/m^3 (20 ppm) CO would result in an increase of COHb of 1.64 percent, and a 5-hour exposure to 12 mg/m^3 would result in an increase of COHb of about 0.7 percent.

Breysse has conducted a study to determine potential health hazards associated with operation of gasoline fork lift trucks in the holds of ships.[25] Carbon monoxide was determined from expired air samples before work, before lunch, after lunch, and after work. Smoking was noted to have a marked effect upon COHb content. Six percent of nonsmokers had COHb levels greater than 3 percent, and 47 percent of 108 smokers exceeded this level prior to work (See Table 9-3). It was further noted that 6 percent of

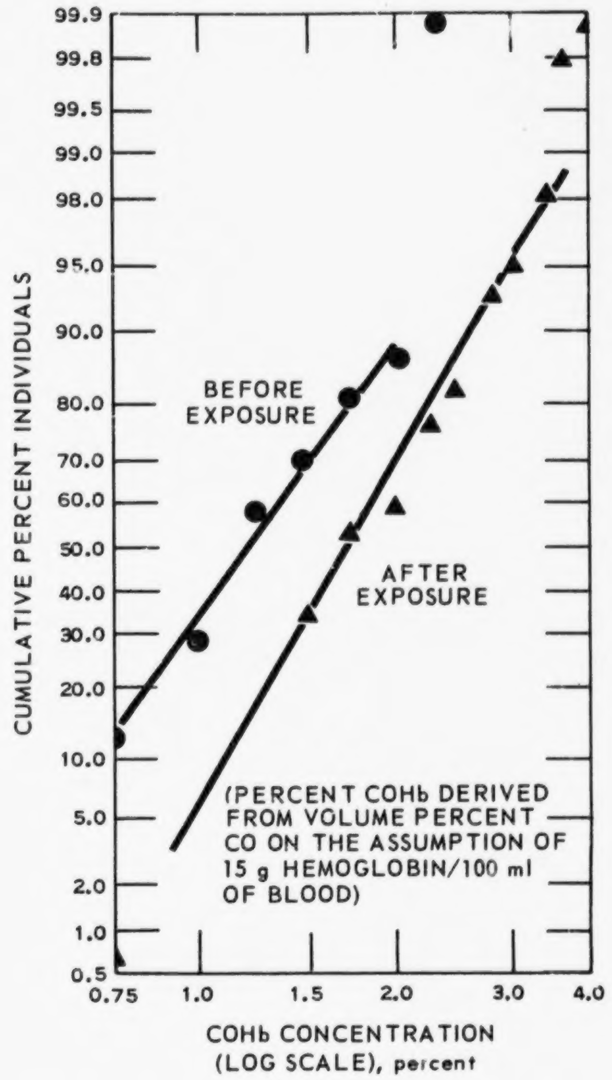

Figure 9-5. COHb levels of policemen who do not smoke before and 5 hours after exposure to between 12 and 23 mg/m^3 (10 and 12 ppm) CO, Paris, 1963.[24]

individuals had COHb levels exceeding 10 percent COHb prior to work, and 10 percent exceeded this level after work. No distinction between smokers and nonsmokers was made in this part of the study.

Airplane pilots flying over forest fires have been studied to determine whether CO exposure significantly affected their COHb.[5] Expired-air analysis indicated that the blood COHb levels averaged 4.5 percent, reaching a maximum of 8.1 percent in one particular pilot. Again, smoking resulted in a higher range of COHb concentration than did occupation.

On the basis of several studies, then, it has been demonstrated that continuous exposure to relatively low levels of CO may result in significant increases in blood COHb levels, for exposure periods as short as 5 hours. Cigarette smoking alone can result in similar or greater increases in COHb levels, and smoking and exposure to ambient levels of CO may both contribute to increasing COHb levels.

3. Cigarette, Pipe, and Cigar Smoke

Carbon monoxide occurs in high concentration in cigarette smoke (greater than 22,400 mg/m^3, 20,000 ppm, or 2 percent), and the average concentration inhaled is about 460 to 575 mg/m^3 (400 to 500 ppm or 0.04 to 0.05 percent).

The magnitude of smoking exposures has been estimated in a population of longshoremen examined prior to the work shift and during periods of little community air pollution.[5] Exposure estimates were based on measurements of CO in expired air after 20-second breathholding. These estimates were validated by measurement of COHb in a sample of the participants. The results are shown in Table 9-4. A level of 5.9 percent COHb was found to be the median value in moderate cigarette smokers who inhale. The relatively low levels in pipe smokers and cigar smokers are due to small amount of smoke inhaled when tobacco is consumed in these forms. The effect of inhaling is clearly to increase the uptake of CO.

Ringold et al. have measured concentrations of CO in expired air and grouped their data according to smoking history.[6] As is shown in Figure 9-6, the amount of CO expired is quite clearly related to smoking habits.

C. DEFINITION OF SENSITIVE GROUPS

The concept of a "susceptible population" merits consideration in the study of air pollution epidemiology. Human responses to community air pollution have shown wide variations, which contribute in no small way to the difficulty in assessing the effects of pollutants. Since air quality criteria must, unless

Table 9-3. COHb LEVELS OF 108 SMOKERS AND 92 NONSMOKERS BEFORE WORK[25]

	Nonsmokers			Smokers		
COHb level, percent	Number	Percent	Cumulative percent	Number	Percent	Cumulative percent
0	26	28	28	3	3	3
1	35	38	66	13	12	15
2	21	23	89	21	19	34
3	4	5	94	20	19	53
4	2	2	96	9	8	61
5	2	2	98	10	9	70
6	2	2	100	18	17	87
7	0	0	100	6	6	93
> 7	0	0	100	8	7	100

Table 9-4. PROPORTION OF SMOKERS AND MEDIAN VALUES OF EXPIRED CO AMONG LONGSHOREMEN[5]

Smoking pattern	Percent of study population by smoking pattern	Median CO, ppm		Median COHb level[a], %	
		Inhaler	Noninhaler	Inhaler	Noninhaler
Never smoked	23.1 (764)[b]	3.2		1.3	
Ex-smoker	12.1 (401)	3.9		1.4	
Pipe and/or cigar smoker only	13.4 (445)	5.4		1.7	
Light smoker (half pack or less per day)	13.0 (429)	17.1	9.0	3.8	2.3
Moderate smoker (more than 1/2 pack and less than 2 packs per day)	31.3 (1,035)	27.5	14.4	5.9	3.4
Heavy smoker (2 packs or more per day)	7.0 (233)	32.4	25.2	6.9	5.5

[a] The percent COHb was estimated from regression.

[b] The number of subjects is given in parentheses. The smoking pattern of four persons was not ascertained.

otherwise specified, consider all of the population rather than just major segments of it, studies must consider especially the impact of air pollution on the "most sensitive" responders. The population group most susceptible to the adverse effects of atmospheric CO can be predicted on a physiological basis to include those persons most sensitive to a decrease in oxygen supply: (1) people with severe anemia due to the already limited supply of oxygen-carrying hemoglobin; (2) those with cardiovascular disease and the resultant impairment of circulation; (3) those with abnormal metabolic states such as thyrotoxicosis or fever, which result in increased oxygen demands; (4) those with chronic pulmonary disease; and, (5) the developing fetus, which may be unusually sensitive to insufficient

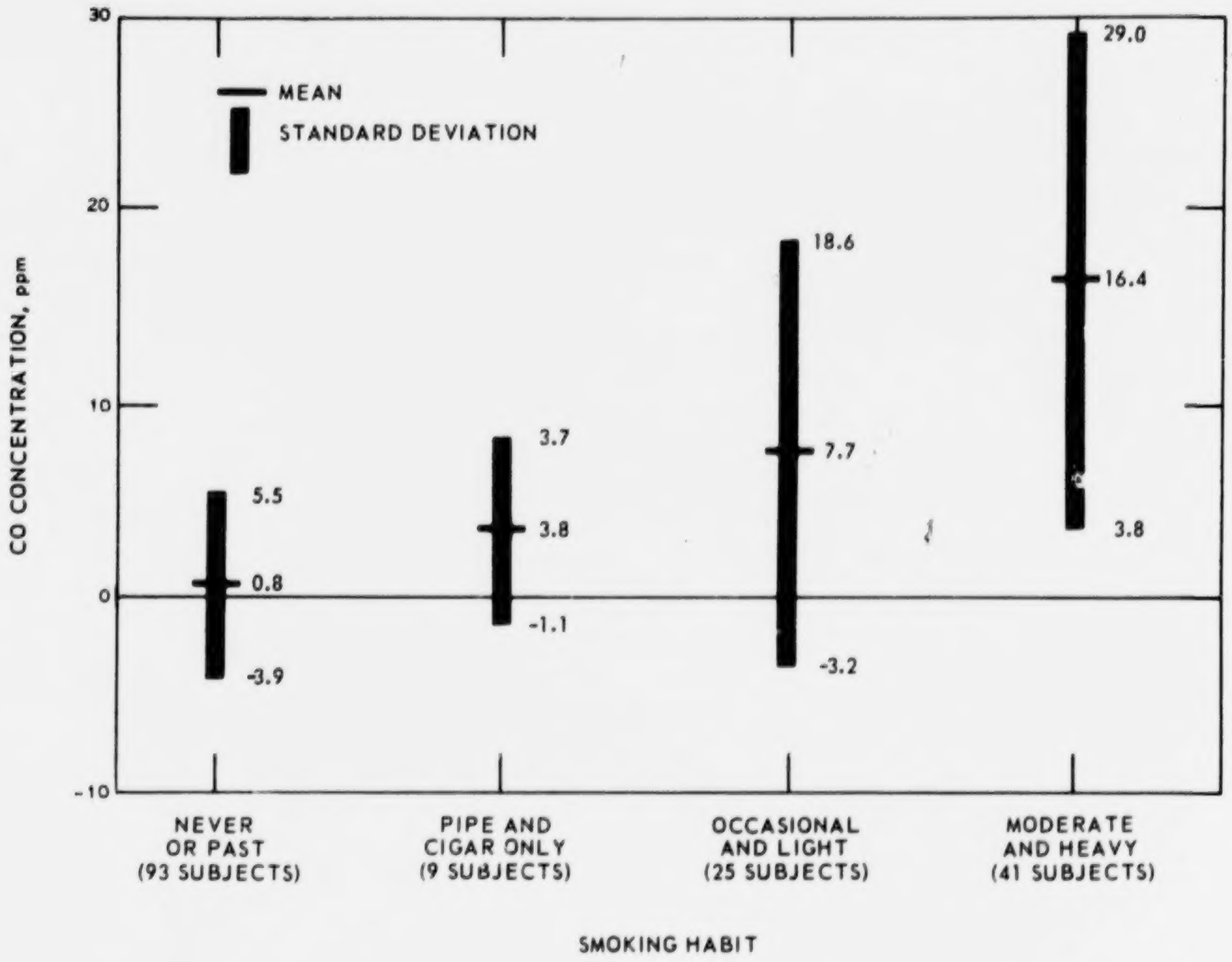

Figure 9-6. Distribution of expired-air CO, according to smoking history and corrected for ambient-air CO.[6]

oxygen. Several recent reviews of the pathophysiology of CO exposure include overviews of the population at greatest risk from such exposure.[26-28] A recent review of animal and human studies strengthens the impression that in patients with insufficient arterial blood flow, small amounts of COHb impair unloading of oxygen and further affect the clinical course.[29]

In addition to the groups proposed as most sensitive, individuals requiring maximal judgmental and functional ability may be an important group to consider in the discussion of health effects associated with CO. Automobile drivers are the largest group of individuals in this category.

A number of studies have pointed out that cigarette smoking may have a deleterious effect upon the fetus, most notably manifest in an increased incidence of low birth weights and a lower average birth weight, but the usual emphasis has been upon components other than CO. Haddon[30] has shown that COHb levels in maternal blood are reflected in the cord blood at delivery. The cord blood of infants delivered from cigarette smoking mothers has a higher COHb level than is found in that of infants from nonsmoking mothers. There appears to be a similar level of COHb in maternal and cord blood (See Figure 9-7). Whether this in itself results in any other effect on the fetus is at this time uncertain, but unborn infants, who during parturition may have exceptional requirements for oxygenation, may well be among the population at high risk.

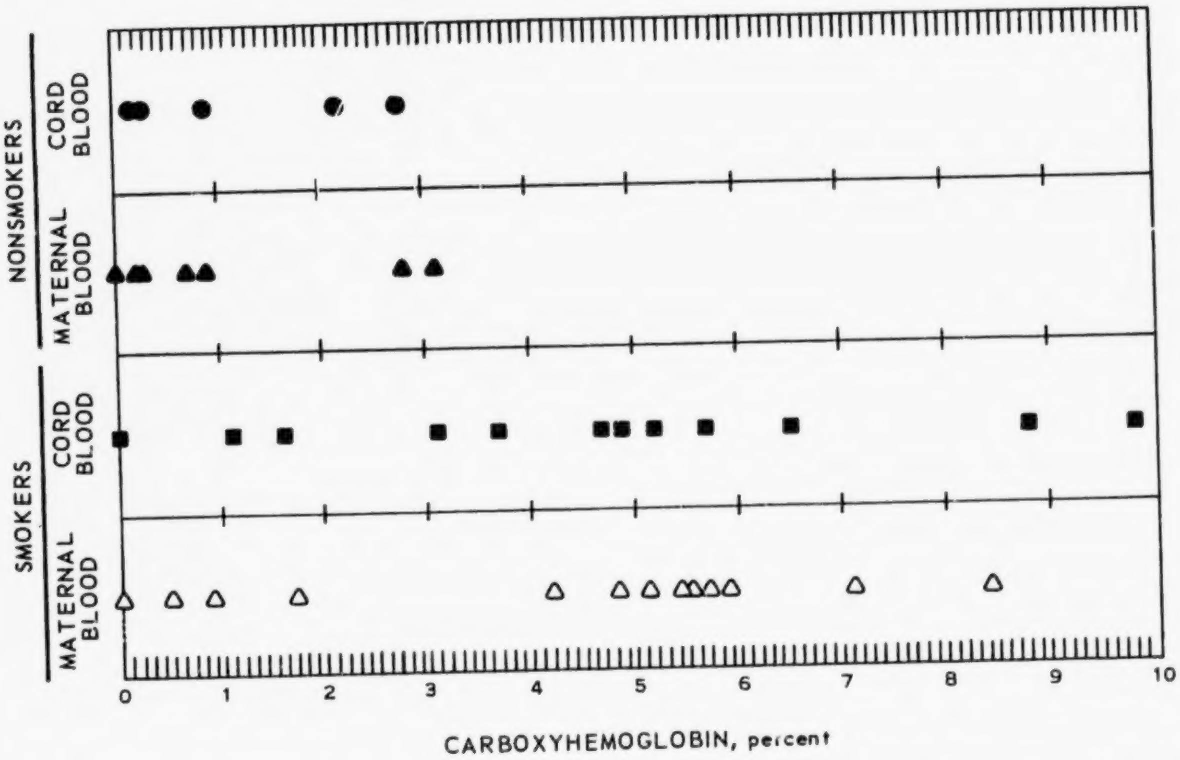

Figure 9-7. Percentage of hemoglobin saturated with CO in cord and maternal blood specimens of smokers and nonsmokers.[30]

D. STUDIES AND INTERPRETATION

1. Mortality Studies

Statistical approaches utilized in determining whether there is excess mortality from atmospheric pollution have been presented by a number of investigators.[31-33] Such variables as particulates, smoke-shade index, oxides of sulfur, and oxidants have been studied with some frequency, but CO has not. This may be due in part to the fact that CO measurements are not always available.

Massey et al. compared mortality in two "communities" in Los Angeles County, which experienced similar daily temperature but different levels of air pollution.[34] The pollutant variables studied were oxidant, SO_2, and CO. The investigators had to compare areas of intermediate and relatively high pollution rather than low versus high areas because it was not possible to maximize differences in air pollution exposure and still remain within an area of uniform temperature. Differences in daily mortality were analyzed by means of correlation and multiple-regression techniques. There were no significant correlations between mortality and pollutant levels. Another problem involved in this use of spatial analysis was the different characteristics of the populations residing within each area. The populations of the communities differed in median age, sex ratio, social status, urbanization, and racial composition. It was hoped in conducting the two-community study that the daily differences between mortality in the low and high area would be relatively independent from day to day. Previous studies have indicated that effects that must be taken into account in time-series analyses are those of autocorrelation as well as cyclic seasonal variations. The negative results of this study must be viewed in light of these limitations.

Using data on cardiac and respiratory mortality for 1956, 1957, and 1958, Hechter and Goldsmith have shown that the number of deaths per day in Los Angeles County varies between 1.0 and 1.3 per 100,000 population.[35] These fluctuations were approximately 180 degrees out of phase with fluctuations for maximal daily temperature and oxidant values, and approximately in phase with CO maxima (See Figure 9-8). If not properly dealt with, such phase differences can produce spurious correlations. When Fourier curves were fitted to the data,* it was found that a single cycle of Fourier functions fit temperature and oxidant levels, and that two-component Fourier curves fit CO levels and cardiorespiratory mortality (See Figure 9-9).

When the residuals from these fitted curves were analyzed, no significant correlations between pollutants and mortality were found (residuals are presumed to have had removed the major effect of time of year). In addition, there were no significant correlations when lag periods of 1 to 4 days were utilized in the analysis. It is possible, however, that in an attempt to remove a time-of-year effect, a real effect of pollutants on mortality may also have been removed, particularly if it was a small effect.

Curphey et al. attempted to determine whether there is any association between the amount of COHb in postmortem blood and ambient CO levels with the 24-hour period preceding death.[36] The investigators were aware of the possibility that postmortem

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*Fourier curve-fitting consists of adding successive pairs of sine and cosine functions as variables, each successive pair being functions of twice the angle of the preceding pair.

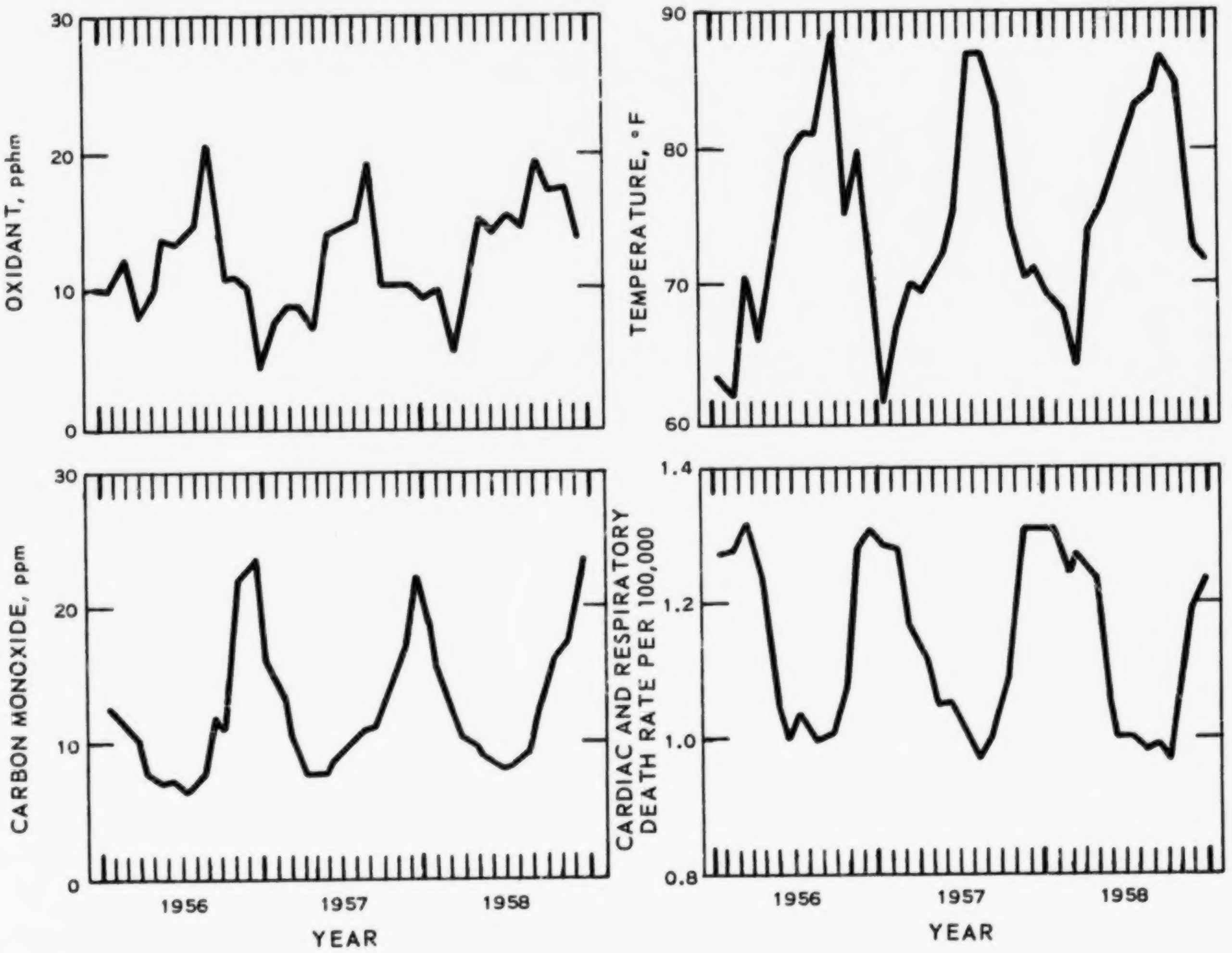

Figure 9-8. Comparison of maximum concentrations of oxidant and carbon monoxide, maximum temperature, and daily death rate for cardiac and respiratory causes, Los Angeles County, 1956-1958.[35]

blood specimens may deteriorate and produce falsely high COHb levels, but they did not find that the length of the interval between death and analysis had any effect on COHb levels in this study.

Information concerning smoking habits was obtained from a questionnaire mailed to next of kin. A total of 1,075 cases for which a COHb determination had been performed was then classified by smoking habits. Nonsmokers consistently had lower COHb levels than smokers. Male nonsmokers had higher COHb levels than female nonsmokers. Variables such as age, time of day and day of week of death, maximum and minimum temperatures, and cause of death had little relationship to COHb levels. There did, however, appear to be some association between ambient CO levels and postmortem COHb levels (See Figure 9-10).

These data have been analyzed further in an attempt to determine whether individuals with cardiovascular disease certified by the coroner's office as having "myocardial infarctions" have different COHb levels than individuals dying of "other cardiovascular disease."[37] Both smokers and nonsmokers were examined initially (Figure 9-11). The myocardial infarction cases were noticed to be younger than those dying of "other cardiovascular disease." Since COHb levels of smokers may diminish with age (either associated with the manner in which cigarettes are inhaled or some other factor that interferes with the alveolar diffusion of CO), an adjustment for age is required when comparisons

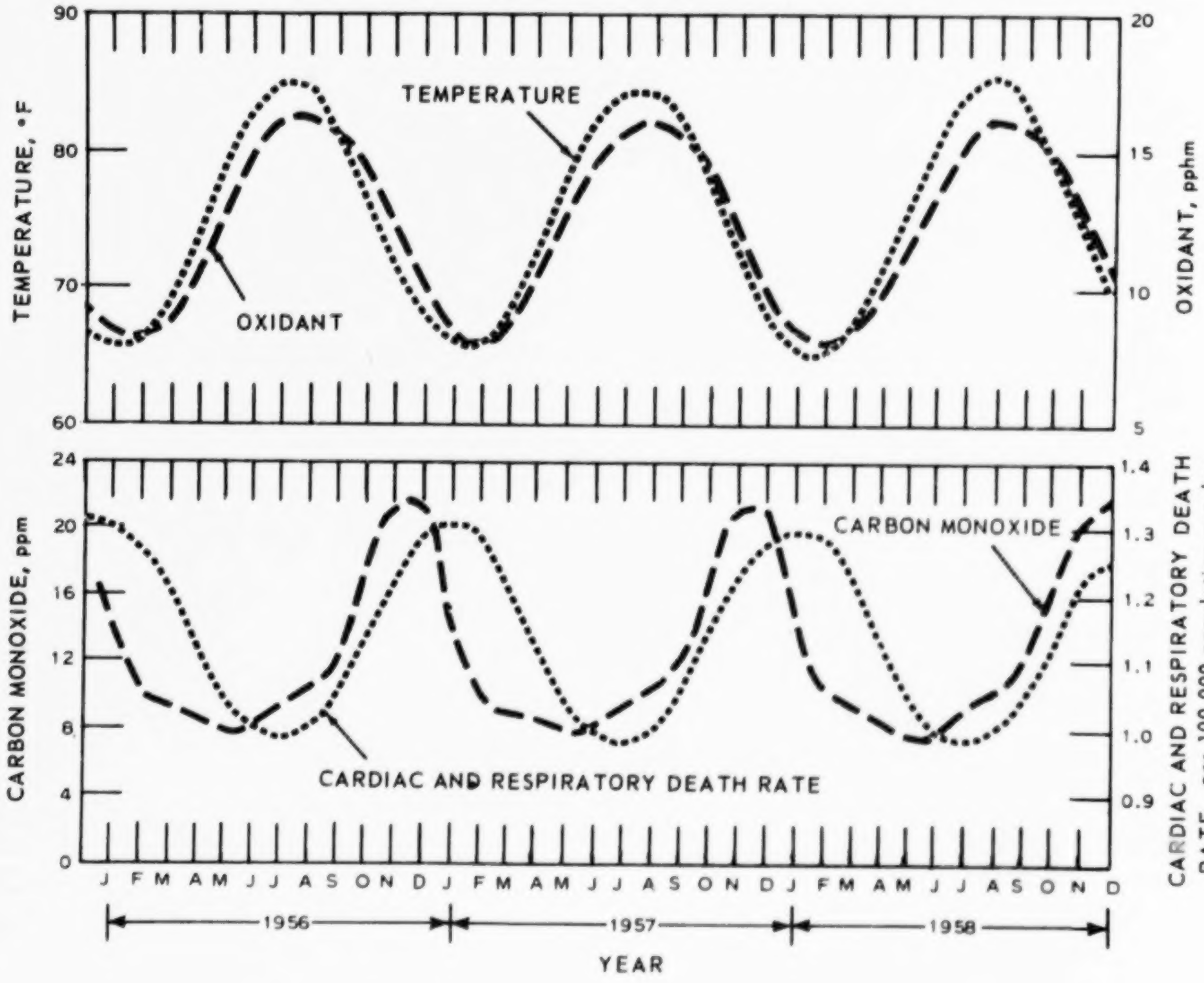

Figure 9-9. Fourier curves fitted to data in Figure 9-8.[15]

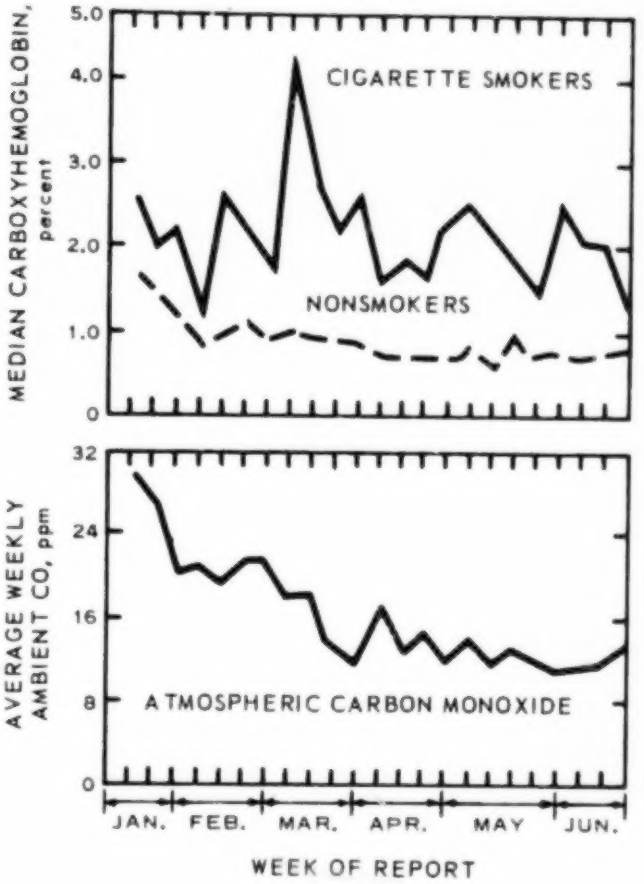

Figure 9-10. COHb levels of coroner cases, by smoking status and atmospheric CO concentrations, Los Angeles County, 1961.[36]

such as these are carried out. When the population was divided into two groups, those 65 and older and those under 65, no significant differences in COHb levels were noted between the two diagnostic categories (Table 9-5). In the male population under age 65, however, the myocardial infarction cases had on the average a higher COHb; but the difference was not significant.

Cohen et al. have attempted to test the hypothesis that during periods of high CO pollution, individuals hospitalized with acute cardiovascular disease are adversely affected.[38] They have studied myocardial infarction admissions to 35 hospitals in Los Angeles County during 1958. Hospital records were abstracted by the medical librarian staff at each hospital. Information obtained included age, sex, date of admission, date of discharge, discharge diagnosis, disposition of patient (recovery or death), area of residence, area of employment, number of days hospitalized, and date of onset of illness. The analysis included 3,080 admissions for myocardial infarction, and involved separate calculations for hospitals in areas of high and low CO pollution.

No significant association was found between the number of admissions for myocardial infarction and ambient CO levels. Significant correlations were found, however, for weekly myocardial infarction case fatality rates and ambient CO levels during the week of admission. Patients admitted to hospitals in the areas of "high" CO pollution where the weekly CO concentration ranged from about 9 to 16 mg/m^3 (8 to 14 ppm) exhibited statistically significant increases ($p<0.01$) in mortality rates from myocardial infarction when compared to patients admitted during weeks with lower average CO concentrations. This correlation was principally accounted for by an end of the year increase in both case fatality rates and ambient CO levels. To avoid spurious correlations, which can result from day-of-week effects as well as autocorrelation, separate analyses were performed for each day of the week and by high and low pollution areas (Table 9-6). Significant associations were then observed only for some of the days of the week and only in the area of the county designated as having high CO levels. The case fatality rates in the high CO area were particularly different from those in the low CO area during weeks of the year with the greatest mean CO levels. The comparability of these two areas was not documented in regard to socioeconomic characteristics.

Factors other than CO exposure, such as hospital admission and hospital-care practices and, most importantly, seasonal influences on case fatality rates, may have accounted for the observed associations. At present, it appears that an association could exist between myocardial infarction case fatality rate and atmospheric CO pollution, but additional studies, particularly of COHb levels in myocardial infarction patients at the time of admission, are required to draw any conclusions about causality. Individuals dying a sudden

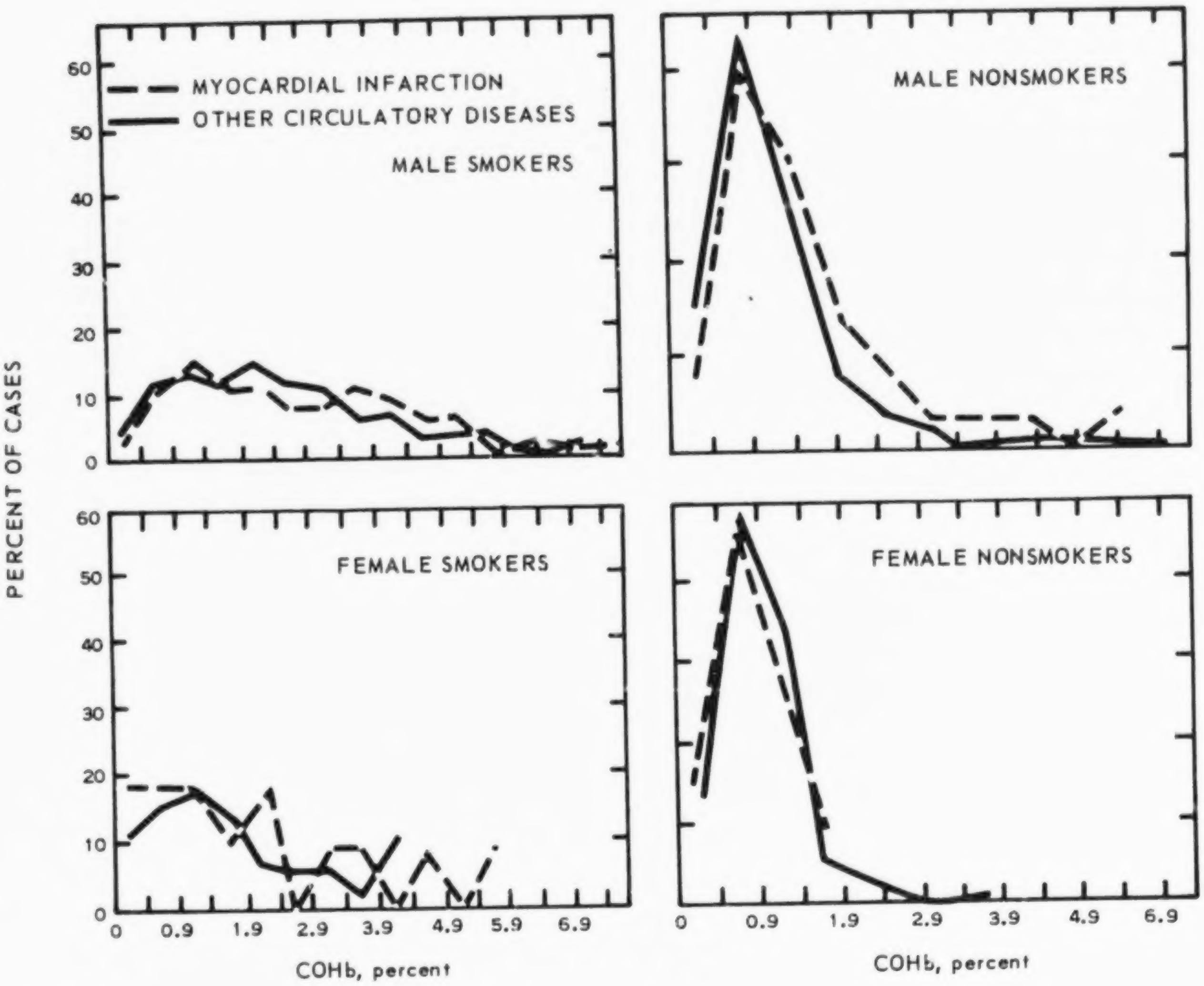

Figure 9-11. COHb levels in myocardial infarction deaths and in other cardiovascular disease deaths, Los Angeles County, 1961.[37]

death and hospitalized myocardial infarction patients must be examined to determine whether the COHb levels of these two populations differ.

2. Morbidity Studies

There have been few studies in which an attempt has been made to relate community CO exposures to indices of health. Instead, the approach utilized has been to study occupationally exposed groups. Because of the limitations of generalizing from occupational groups to the general population as previously discussed, community morbidity studies are becoming increasingly important.

Cassell et al. obtained daily records of illness prevalence from a panel of 1,747 persons living within a restricted geographic area of New York City.[39] The subjects were followed at weekly intervals for an average of 45 weeks each, providing 61,000 person-weeks of information. Symptoms recorded were common cold, cough, headache, and eye irritation. Pollutants under study included particulate matter, total hydrocarbons, CO, and sulfur dioxide. Meteorologic factors such as wind speed, precipitation, and temperature were also considered. Correlation analyses demonstrated two distinct clusters of environmental variables and their associated symptoms. Headache and eye irritation tended to occur with warm, humid weather and stagnant meteorologic conditions in which there were high levels of CO, ammonia, aldehydes, total

Table 9-5. COHb LEVELS FOR CARDIOVASCULAR DISEASE CATEGORIES BY AGE, SMOKING HABITS, AND SEX,[a] LOS ANGELES COUNTY, 1961[37]

Age group and cause of death	Smoker						Nonsmoker					
	Male			Female			Male			Female		
	Mean COHb	S D	Number of cases	Mean COHb	S D	Number of cases	Mean COHb	S D	Number of cases	Mean COHb	S D	Number of cases
Under 65 years												
Myocardial infarction	3.13	1.70	76	(2.10)[b]	1.84	8	1.44	1.30	14	(0.70)[b]	0.22	5
Other circulatory	2.84	1.52	116	3.01	2.43	24	1.15	0.83	45	0.76	0.40	27
65 and older												
Myocardial infarction	1.29	0.64	15	(2.23)[b]	2.81	3	1.18	0.86	23	0.91	0.50	15
Other circulatory	2.02	1.40	80	1.43	1.09	26	0.98	0.69	154	0.92	0.52	194

[a] None of differences within sex, age, and smoking category are statistically significant.

[b] Parentheses indicate mean based on samples smaller than 10 cases.

Table 9-6. RELATIONSHIP BETWEEN NUMBER OF HOSPITAL ADMISSIONS FOR MYOCARDIAL INFARCTION, MYOCARDIAL INFARCTION CASE FATALITY RATES, AND AMBIENT CO LEVELS BY DAY OF WEEK, LOS ANGELES COUNTY, 1958[38]

Day of admission	Avg CO concentration, ppm	Total area				High area		Low area	
		Mean myocardial infarction admissions	Correlation[a] coefficient-admissions versus CO	Mean case fatality rate per 100 admissions	Correlation[b] coefficient-case fatality rate versus CO	Mean case fatality rate per 100 admissions	Correlation[a] coefficient-case fatality rate versus CO	Mean case fatality rate per 100 admissions	Correlation[a] coefficient-case fatality rate versus CO
All days	7.41	8.46	0.002	26.0	0.114[c]	27.3	0.162[d]	19.1	-0.002
Weekdays	7.66	8.94	-0.120	24.7	0.130[c]	25.8	0.167[d]	18.4	0.048
Weekends	6.80	7.26	-0.022	30.2	0.177	31.7	0.256[d]	22.0	-0.101
Sunday	6.53	6.94	-0.251	28.3	0.049	29.3	0.037	22.8	0.011
Monday	7.71	9.54	-0.234	25.4	0.019	26.3	0.058	11.7	0.093
Tuesday	7.45	9.41	-0.071	23.5	0.134	24.5	0.096	21.8	0.209
Wednesday	7.53	9.13	0.150	24.2	0.273[c]	24.7	0.186	24.1	0.207
Thursday	7.71	8.08	-0.019	26.9	-0.030	29.4	0.210	18.4	0.161
Friday	7.90	8.56	0.121	23.6	0.262	24.3	0.308[c]	23.5	-0.111
Saturday	7.07	7.58	-0.040	32.0	0.309[c]	34.0	0.466[c]	21.2	-0.182

[a] Correlation between myocardial infarction admissions and log CO (basin average).

[b] Correlation between arc sin transformation of myocardial infarction case fatality rate ($x^1 = \text{arc sin}\sqrt{\frac{x+1}{N+1}} + \text{arc sin}\sqrt{\frac{x}{N+1}}$) where x is the number of deaths and N is the number of admissions and log CO (basin average).

[c] Significant at the 5% level.

[d] Significant at the 1% level.

oxidants, and organic acids, but low levels of hydrocarbons and sulfur dioxide. The second cluster of effects (common cold, cough, and sore throat) were thought to occur in wintry weather (low radiation, low humidity, low temperature, and medium winds) with high levels of particulate matter and oxides of sulfur, but virtually no oxidant or aldehydes. The relevance of this work to actual effects of CO is limited since the presence of CO was probably only an index of a variety of primary pollutants. The association of headache and increased ambient CO concentrations is, however, quite plausible.

Sterling[3,4] et al. assembled Blue Cross admissions data from Los Angeles hospitals for the period March to October 1961. Diagnoses were grouped according to what the authors consider "highly relevant," "relevant," and "nonrelevant" illnesses. After correcting for day-of-week effects in both pollutant and admission frequencies, a statistically significant correlation was found with CO and several other pollutants for "highly relevant" conditions such as allergic disorders, inflammatory diseases of the eye, acute upper respiratory infections, influenza, and bronchitis. Since there is no biologically plausible explanation for such an association, at the present time such a relationship cannot be regarded as significant in terms of CO.

Verma[40] et al. undertook a retrospective study of absences due to illness among a group of white-collar workers located in metropolitan New York during a 3-year period. Any employee who had been absent because of illness reported to the company medical department for appraisal prior to his returning to work. These records were then categorized as either respiratory or nonrespiratory illness, and an association was noted between respiratory illness and ambient sulfur dioxide levels. No such association was observed between respiratory illness and CO. No association was found between nonrespiratory illness and sulfur dioxide, smoke shade, or CO. When time trends were removed from the data and analyses were repeated, there were no significant associations between absences and any of the pollution variables. These data therefore demonstrate yearly cyclic behavior, which tends to influence both pollutants and illness absences. The authors state the models they have developed retain their descriptive power for respiratory illness absences, and suggest that while no causal association can be inferred, there is a relationship between respiratory illness absences, air pollution, and climate variables from one time period to the next.

3. Possible Relevance of Carbon Monoxide Exposure to Motor Vehicle Accidents

As noted in the prior section dealing with magnitude and types of exposure, motor vehicles contribute a large proportion of community CO exposure. The effects of CO upon visual threshold and ability to discriminate time intervals[41, 42] have been discussed in detail in Chapter 3, Section E. In view of the increasing evidence of sensory impairment associated with relatively low-level CO exposures, it has become quite pertinent to determine whether such effects in motor vehicle drivers predispose them to accidents. McFarland has reviewed the numerous factors that must be taken into account in epidemiologic studies of motor vehicle accidents.[43,44]

During the period 1959 through 1963 Chovin[24] determined COHb levels in three population groups. He analyzed 1,672 blood samples from motor vehicle drivers who were thought to be responsible for accidents, 3,818 samples from workers who were sometimes exposed to CO in their occupations, and 1,518 samples from individuals who were suspected of having been exposed to domestic sources of CO. Alcohol measurements were also made in the accident category, but data are not available. The cumulative distribution of blood CO levels is shown in Figure 9-12. Individuals involved in auto accidents had the highest blood CO levels, followed by workers with CO exposure; individuals with suspected exposure to CO in the home had the lowest blood CO levels. Chovin notes that smokers and nonsmokers were present in all three categories, but no data are presented to indicate

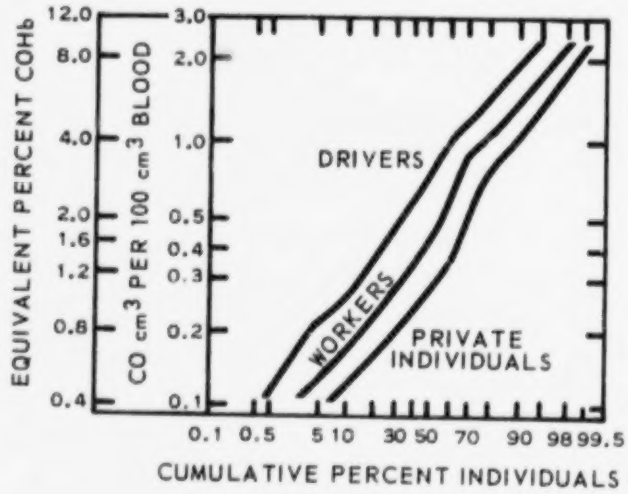

Figure 9-12. Cumulative distribution of blood CO concentrations, based on 5-year study of car drivers, workmen with CO exposure, and private individuals suspected of accidental CO exposure.[24]

whether the proportion of smokers and nonsmokers is the same in these categories. Other questions, especially the association of increased cigarette consumption with other variables, must be dealt with before any firm conclusions can be drawn from this study.

An additional approach that could be of assistance in determining the relevance of CO to automobile accidents is study of the frequency of motor vehicle accidents during periods of and in locations with different CO levels. A statistical and epidemiological strategy for this purpose has been developed and utilized by Ury[45] for studying the effect of oxidant on automobile accidents.

E. SUMMARY

Exposures to environmental levels of CO can increase blood COHb concentrations in human subjects. The amount of this increase is reasonably predictable and must be considered in relation to CO exposures from inhaled cigarette smoke as well as from occupational and domestic sources. Methods for estimating COHb levels in large populations are relatively simple.

Continuous exposure to relatively low levels of CO may result in significant increases in blood COHb levels for exposure periods of only a few hours. Such an exposure increases the body burden of COHb in persons who do not already have such a body burden from cigarette smoking. Longer exposures would most likely produce a somewhat greater increase, with greater potential for impairment of tissue oxygenation.

Exposure of traffic policemen, in Paris, for 5 hours to between 12 and 14 mg/m^3 (10 and 12 ppm) increased COHb levels in nonsmokers by about 0.7 percent. The same exposures of cigarette smokers may cause those who have elevated COHb at the start of exposure to have a decrease in COHb and those who had relatively low values of COHb at the start of the study to have an increase in COHb. Cigarette smoking was not permitted during this 5-hour period of exposure.

Apart from increases in COHb, three possible effects have been a source of major consideration in epidemiologic studies:

1. Continued exposure to low levels of CO may produce some persistent toxic reaction, such as a chronic CO poisoning syndrome. The evidence for the occurrence of such a condition is inadequate and is based primarily on subjective symptons.
2. The evidence to date, though inconclusive, suggests that weekly average CO values in excess of from 9 to 16 mg/m^3 (8 to 14 ppm) may be associated with an increase in mortality in hospitalized patients with myocardia infarction. Substantiation of this impression will require a study of the prognosis of myocardial infarction patients in relationship to COHb levels measured at admission to the hospital
3. In two studies, persons driving motor vehicles that were involved in accidents had higher COHb levels than "control" populations; controls were not ideal, however. Possible mechanisms by which CO might affect the ability to drive a motor vehicle are suggested in the available data in CO

effects upon visual sensitivity, psychological test performance, and accurate estimation of time intervals. As little as 2.5 percent COHb has produced these effects in laboratory studies of nonsmokers, and the available epidemiologic information is consistent with the premise that such an increase in COHb levels among drivers might influence the frequency of accidents.

Specific areas wherein research is needed to clarify uncertainties relating to health effects of CO exposure are:

1. The increment of COHb that can be produced by exposures to CO concentrations in the range of 12 to 23 mg/m^3 (10 to 20 ppm) for time periods from 8 to 24 hours.
2. The relationship of ambient CO levels and of COHb levels to the survival of hospitalized patients with myocardial infarction.
3. The prognostic significance with respect to cardiovascular conditions of elevated levels of COHb.
4. The relationship, if any, between ambient CO and COHb levels and the occurrence of motor vehicle accidents when weather and driving conditions, cigarette smoking, alcohol and drug use, and other factors are adjusted and controlled.
5. The relationship between concentrations of CO measured outdoors and inside households.

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CHAPTER 10.

SUMMARY AND CONCLUSIONS

A. OCCURRENCE, PROPERTIES, AND FATE OF ATMOSPHERIC CARBON MONOXIDE

Because of its origin from the incomplete combustion of organic materials, carbon monoxide (CO) is emitted to the atmosphere in greater quantities than any other urban air pollutant. The largest sources of CO in the urban environment may be classified as technological. Several geophysical and biological sources of this pollutant have been identified, but their contribution to urban atmospheric concentrations is thought to be small. Background concentrations of CO (arising from both natural and technological sources) are presently estimated to range from 0.029 to 1.15 milligrams per cubic meter (mg/m^3), i.e., 0.025 to 1.00 part per million (ppm).

Carbon monoxide is a colorless, odorless, tasteless gas. Oxidation of CO to carbon dioxide (CO_2) does occur in the atmosphere, but the rate of the known reactions have been shown to be very slow. The mean residence time of atmospheric CO has been estimated to be between 1 month and 5 years.

Removal processes for atmospheric CO have been postulated to include: the migration of CO to the upper atmosphere, the binding of CO to porphyrin compounds in plants and animals, and undetermined interactions between CO and ocean water, and the adsorption and oxidation of CO on various surfaces. Some of these removal processes are, however, highly speculative.

B. FORMATION OF CARBON MONOXIDE

CO arises primarily from incomplete or inefficient combustion of carbonaceous fuels. Oxygen concentration, flame temperature, gas residence time, and combustion chamber turbulence are important variables that affect the exhaust concentrations of CO.

C. ESTIMATION OF CARBON MONOXIDE EMISSIONS

An estimated 92 x 10^9 kilograms (102 million tons) of CO were emitted in the United States in 1968. This amounts to 50 percent by weight of all major air pollutant emissions that year. Fuel combustion in mobile sources utilizing the internal combustion engine is the principal source category of CO (58 percent). Miscellaneous combustion sources, principally forest fires, and industrial process sources are the second (17 percent) and third (11 percent) largest categories, respectively. Disposal of solid wastes is the fourth (8 percent) greatest source category of CO emissions, and stationary fuel combustion is the fifth (2 percent).

Emission estimates were derived by the use of emission factors and activity levels. A summary of the method of estimation applied to each source category is presented. Estimates indicate that no further increase in magnitude of CO vehicular emissions above the 1968 value of 59 million tons would be expected before about 2000.

D. MEASUREMENT OF CARBON MONOXIDE CONCENTRATIONS IN AMBIENT AIR

Nondispersive infrared (NDIR) analyzers are the most commonly used continuous, automated devices for measuring atmospheric CO concentrations and are generally accepted as the most reliable reference method. Measuring ranges usually extend from 1 to 58 mg/m^3 (1 to 50 ppm) CO or from 1 to 115 mg/m^3 (1 to 100 ppm) CO. Water vapor and CO_2 interfere in the determination of CO by NDIR techniques. Filter cells and treatment of the incoming gas stream are techniques used to minimize these interferences.

Galvanic and coulometric analyzers are two other instruments commercially available for continuously measuring CO concentrations. The function of both instruments depends on the oxidation of CO by iodine pentoxide (I_2O_5). These instruments are flow- and temperature-dependent and suffer from multiple interferences; consequently, they have not been widely used.

A mercury vapor analyzer, which depends on the liberation of mercury vapor when CO is passed over hot mercuric oxide, has been used as a portable, continuous-monitoring analyzer. Though especially adaptable for measuring low CO concentrations [0.29 mg/m^3 (0.25 ppm)], this instrument does not appear suitable for routine air monitoring because of numerous interferences and electronic instability.

A recently developed automated gas chromatographic system operates by quantitatively converting CO to methane (CH_4), which is subsequently semi-continuously measured by a flame ionization detector. This arrangement shows considerable promise as a monitoring device. Concentrations of from 0.1 to 1,150 mg/m^3 (0.1 to 1,000 ppm) may be determined, and instrument output over this range is linear for both CO and CH_4.

Another principle for determination of atmospheric CO concentrations is based on the catalytic conversion, using Hopcalite, of CO to CO_2 with a measurement of the resulting temperature rise. These systems are widely used in enclosed spaces, but their applicability for ambient air monitoring is limited because they function best at high ambient concentrations.

Intermittent samples may be collected in the field and later analyzed in the laboratory by NDIR, gas chromatographic, or infrared spectrophotometric methods of analysis. Colorimetric techniques, generally based on the reduction of a metallic salt, have been used for rapid, relatively gross estimates of CO concentrations.

Accurately prepared standard samples are necessary for the calibration of any instrument used to measure CO concentrations. Gas samples may be standardized by volumetric, gravimetric, and chemical techniques.

E. ATMOSPHERIC CARBON MONOXIDE CONCENTRATIONS

Diurnal, weekly, and seasonal variations in CO concentrations can be observed. Diurnal and weekly variations correlate best with community traffic patterns; seasonal variations are most dependent on meteorologic variables.

Both macro- and micrometeorological factors play a role in the rate of dispersion of CO emissions. Micrometeorological factors, such as mechanical turbulence produced by automobiles and airflow around buildings, become important in determining street-side exposures. Macrometeorological factors can lead to air stagnation, which causes high community CO levels.

The concepts of averaging time and frequency of occurrence are important when describing ambient pollutant measurements. Because of physiological considerations, the averaging time of most interest for CO is 8 hours. Aerometric data from the Continuous Air Monitoring Program, the State of California, and Los Angeles County were analyzed for the 8-hour-averaging-time CO concentration exceeded 0.1 percent of the time at each available site. These values ranged from approximately 12 to 46 mg/m^3 (10 to 40 ppm).

To aid in analyzing aerometric data, a statistical model has been developed. While year-to-year mean and peak CO values may vary markedly within a community, the model can be used to calculate, based on any averaging time, a statistically probable annual maximum concentration.

Within a community, CO concentrations vary markedly with location. Calculated annual maximum concentrations in the most polluted 5 percent of the locations incorporated in a recent sample of a variety of sites showed that CO concentrations predicted inside the passenger compartment of motor vehicles in downtown traffic were almost 3 times those predicted in central urban areas and 5 times those expected in residential areas. Occupants of vehicles traveling on expressways and arterial routes were found to have CO exposures somewhere between those in central urban areas and in downtown traffic.

Concentrations exceeding 100 mg/m^3 (87 ppm) have been measured in underground garages, in tunnels, and in buildings constructed over highways.

Using emission and meteorological data, diffusion models can be used to estimate community air quality under a variety of conditions.

F. EFFECTS OF CARBON MONOXIDE ON VEGETATION AND MICROORGANISMS

Plants are relatively insensitive to CO at the lower levels of concentrations that have been found to be toxic for animals. CO has not been shown to produce detrimental effects on certain higher plants at concentrations below 115 mg/m^3 (100 ppm) when exposed for from 1 to 3 weeks. Nitrogen fixation by *Rhizobium trifolii* innoculated into red clover plants has been reduced by about 20 percent, however, after exposure to 115 mg/m^3 (100 ppm) CO for 1 month.

G. TOXICOLOGICAL APPRAISAL OF ATMOSPHERIC CARBON MONOXIDE

CO is absorbed by the lung and reacts primarily with hemoproteins and most notably with the hemoglobin of the circulating blood. The absorption of CO is associated with a reduction in the oxygen-carrying capacity of blood and in the readiness with which the blood gives up its available oxygen to the tissues. The affinity of hemoglobin for CO is over 200 times that for oxygen, indicating that carboxyhemoglobin (COHb) is a more stable compound than oxyhemoglobin (O_2Hb). About 20 percent of an absorbed dose of CO is found outside of the vascular system, presumably in combination with myoglobin and heme-containing enzymes. The magnitude of absorption of CO increases with the concentration, the duration of exposure, and the ventilatory rate. With fixed concentrations and with exposures of sufficient duration, an equilibrium is reached; the equilibrium is reasonably predictable from partial-pressure ratios of oxygen to CO.

Long-term exposures of animals to sufficiently high CO concentrations can produce structural changes in the heart and brain. It has not been shown that ordinary ambient exposures will produce this. The lowest exposure producing any such changes has been 58 mg/m^3 (50 ppm) continuously for 6 weeks.

The normal or "background" concentration of COHb in nonsmokers is about 0.5 percent and is attributed to endogenous sources such as heme catabolism. The body's uptake of exogenous CO increases blood COHb according to the concentration and length of exposure to CO as well as the respiratory rate of the individual.

In human exposure studies, continuous exposure to 35 mg/m^3 (30 ppm) CO has led to 80 percent of the equilibrium value of 5 percent COHb being approached in 4 hours, and the remaining 20 percent approached slowly over the next 8 hours. Theoretical calculations indicate a COHb equilibrium value of about 3.7 percent after continuous exposure to 23 mg/m^3 (20 ppm) and about 2 percent after continuous exposure to 12 mg/m^3 (10 ppm). The equilibrium values are generally reached after about 8 or more hours of exposure, although physical activity can shorten this time period.

Interference with the accurate estimation of time intervals has been demonstrated in nonsmokers with exposures to as low as 58 mg/m^3 (50 ppm) CO for 90 minutes. Such an exposure is likely to lead to COHb levels in the range of 2.5 percent. At a blood level of about 3 percent COHb, estimated by expired air analysis after exposure of nonsmokers to 58 mg/m^3 (50 ppm) CO for 50 minutes, significant changes in relative brightness threshold and visual acuity have been observed. Evidence of impairment in performance of other psychomotor tests has been associated with COHb levels of 5 percent in some instances. Experimental exposures of human subjects to CO leading to blood COHb levels above 5 percent have been associated with impairment in the oxidative metabolism of the myocardium in subjects with pulmonary emphysema and coronary heart disease. Persons in the latter group are unable to compensate for CO exposures by increasing coronary blood flow and are, therefore, particularly vulnerable. Persons with veno-arterial shunts in the circulation are also probably vulnerable, as are those with respiratory impairment. From physiologic considerations CO would be expected to have a greater effect with increasing altitude.

There is evidence that CO exposure increases the hematocrit of the blood and probably the circulating blood volume, although the significance of these changes is not clear. There is evidence that prolonged exposure to relatively high concentrations of CO increases the deposition of lipids in the major blood vessels of rabbits, and this could be a factor in the pathogenesis of arteriosclerosis.

Thus, in summary it may be stated that: (1) no human health effects have been demonstrated for COHb levels below 1 percent, since endogenous CO production makes this a physiological range; (2) the following effects on the central nervous system occur above 2 percent COHb: (a) at about 2.5 percent COHb in nonsmokers (from exposure to 58 mg/m^3 for 90 minutes), an impairment in time-interval discrimination, has been documented, (b) at about 3 percent COHb in nonsmokers (from exposure to 58 mg/m^3 for 50 minutes), an impairment in visual acuity and relative brightness threshold has been observed, (c) at about 5 percent COHb there is an impairment in performance of certain other psychomotor tests; (3) cardiovascular changes have been shown to occur at exposure sufficient to produce over 5 percent COHb; they include increased cardiac output, increased arterial-venous oxygen difference, increased coronary blood flow in patients without coronary disease, decreased coronary sinus blood P_{O_2} in patients with coronary heart disease, impaired oxidative metabolism of the myocardium, and other related effects; these changes have been demonstrated to produce an exceptional burden on some patients with heart disease; and (4) adaptation to CO may occur through increasing blood volume, among other mechanisms.

H. EPIDEMIOLOGICAL APPRAISAL OF CARBON MONOXIDE

Those segments of the population most susceptible to the adverse effects associated with atmospheric CO can be predicted on a physiologic basis to include those people most sensitive to a decreased oxygen supply. These susceptible groups include, then, individuals with anemia, cardiovascular disease, anormal metabolic states such as thyrotoxicosis or fever, and chronic pulmonary disease and the developing fetus.

A major source of CO exposure is cigarette smoke; cigarette smokers generally have a COHb with a median value of 5 percent, whereas nonsmokers are usually found to have about 0.5 percent COHb. Community exposures of people who are cigarette smokers and already have an elevated COHb will either lead to an increase in COHb or will slow down the excretion of CO during intervals between cigarette smoking, depending upon the initial COHb level in the smoker and the magnitude and duration of the ambient CO exposure. Exposure of traffic policemen, in Paris, for 5 hours to between 12 and 14 mg/m^3 (10 and 12 ppm) has increased COHb levels in nonsmokers by about 0.7 percent. The extent of human CO exposure from sources other than smoking or the ambient outdoor air has not been well documented.

Several effects of long-term exposure to CO have been implicated. Recent data suggest that the mortality from myocardial infarction may be increased by exposure to average weekly CO concentrations of from 9 to 16 mg/m^3 (8 to 14 ppm), although these results are not conclusive and require replication. The probability of involvement in motor vehicle accidents may also be associated with CO exposure. This could be related to the influence of CO exposure on visual acuity, estimation of time intervals, or other psychomotor parameters.

I. AREAS FOR FUTURE RESEARCH

Review of this document reveals many areas where additional research is necessary to fill the gaps in our present knowledge of the behavior and effects of ambient CO.

The atmospheric reactions and fate of ambient CO are only vaguely understood and therefore require further study. Improvements are needed in instrument-measuring methods, particularly with a view to eliminating interferences and to making the instruments less cumbersome. Associated with this is the need to measure the influence of outdoor CO levels on indoor CO concentrations.

Research on the physiology of CO in the human body has provided considerable information on both endogenous CO production and on the effects of CO at various cellular and microcellular levels. Our knowledge of the effects of CO on enzyme systems and tissue oxygenation, however, is far from complete. In addition, mechanisms of CO catabolism in the body remain undefined. The uptake of CO during varying time periods and with changes in activity must be further documented.

Studies of the effects of CO on human behavior and performance need both clarification and replication. Definition and sophistication of parameters sensitive to changes in blood carboxyhemoglobin merit considerable attention as a prerequisite to better defining the influence of CO on human performance.

Epidemiological information is urgently needed on the possible effects of CO on several segments of the population which theoretically at least are at great risk to CO exposure. In addition, many questions have been raised concerning the relationship between CO exposure and the development and/or progression of cardiovascular disease, and our present state of knowledge is far from complete on this subject.

The relationship between CO exposure from smoking and CO exposure from the ambient air is not clear at the present time. While both exposures produce increases in blood COHb, the associated effects are not identical. Whether or not some method of adaptation to CO exposure exists is a debatable issue at the present time.

J. CONCLUSIONS

Derived from a careful evaluation of the studies cited in this document, the conclusions given below represent the National Air Pollution Control Administration's best judgment of the effects that may occur when various levels of pollution are reached in the ambient air. Additional information from which the conclusions were derived, and qualifications that may enter into consideration of these data, can be found in the appropriate chapter of this document.

1. Experimental exposure of nonsmokers to a concentration of 35 mg/m^3 (30 ppm) for 8 to 12 hours has shown that an equilibrium value of 5 percent COHb is approached in this time; about 80 percent of this equilibrium value, i.e., 4 percent COHb, is present after only 4 hours of exposure. These experimental data verify formulas used for estimating the equilibrium values of COHb after exposure to low concentrations of CO. These formulas indicate that continuous exposure of nonsmoking sedentary individuals to 23 mg/m^3 (20 ppm) will result in a blood COHb level of about 3.7 percent, and an exposure to 12 mg/m^3 (10 ppm) will result in a blood level of about 2 percent (Chapter 8, Sections D and K).

2. Experimental exposure of nonsmokers to 58 mg/m^3 (50 ppm) for 90 minutes has been associated with impairment in time-interval discrimination (See Chapter 8, Section E). This exposure will produce an increase of about 2 percent COHb in the blood. This same increase in blood COHb will occur with continuous exposure to 12 to 17 mg/m^3 (10 to 15 ppm) for 8 or more hours. (See Chapter 8, Sections D and E).
3. Experimental exposure to CO concentrations sufficient to produce blood COHb levels of about 5 percent (a level producible by exposure to about 35 mg/m^3 for 8 or more hours) has provided in some instances evidence of impaired performance on certain other psychomotor tests, and an impairment in visual discrimination (Chapter 8, Section E).
4. Experimental exposure to CO concentrations sufficient to produce blood COHb levels above 5 percent (a level producible by exposure to 35 mg/m^3 or more for 8 or more hours) has provided evidence of physiologic stress in patients with heart disease (Chapter 8, Section F).

Table 10-1 presents these conclusion in tabular form.

K. RESUMÉ

An exposure of 8 or more hours to a carbon monoxide concentration of 12 to 17 mg/m^3 (10 to 15 ppm) will produce a blood carboxyhemoglobin level of 2.0 to 2.5 percent in nonsmokers. This level of blood carboxyhemoglobin has been associated with adverse health effects as manifested by impaired time interval discrimination. Evidence also indicates that an exposure of 8 or more hours to a CO concentration of 35 mg/m^3 (30 ppm) will produce blood carboxyhemoglobin levels of about 5 percent in nonsmokers. Adverse health effects as manifested by impaired performance on certain other psychomotor tests have been associated with this blood carboxyhemoglobin level, and above this level there is evidence of physiologic stress in patients with heart disease.

There is some epidemiological evidence that suggests an association between increased fatality rates in hospitalized myocardial infarction patients and exposure to weekly average CO concentrations of the order of 9 to 16 mg/m^3 (8 to 14 ppm).

Evidence from other studies of the effects of CO does not currently demonstrate an association between existing ambient levels of CO and adverse effects on vegetation, materials, or other aspects of human welfare.

It is reasonable and prudent to conclude that, when promulgating air quality standards, consideration should be given to requirements for margins of safety that would take into account possible effects on health that might occur below the lowest of the above levels.

Table 10–1. EFFECTS OF CARBON MONOXIDE

Environmental conditions	Effect	Comment	Reference
35 mg/m^3 (30 ppm) for up to 12 hours	Equilibrium value of 5 percent blood COHb is reached in 8 to 12 hours; 80 percent of this equilibrium value, (4 percent COHb) is reached within 4 hours.	Experimental exposure of nonsmokers. Theoretical calculations suggest exposure to 23 (20 ppm) and 12 mg/m^3 (10 ppm) would result in COHb levels of about 3.7 and 2 percent, respectively, if exposure was continuous for 8 or more hours.	Smith
58 mg/m^3 (50 ppm) for 90 minutes	Impairment of time-interval discrimination in nonsmokers.	Blood COHb levels not available, but anticipated to be about 2.5 percent. Similar blood COHb levels expected from exposure to 10 to 17 mg/m^3 (10 to 15 ppm) for 8 or more hours.	Beard and Wertheim
115 mg/m^3 (100 ppm) intermittently through a facial mask	Impairment in performance of some psychomotor tests at a COHb level of 5 percent.	Similar results may have been observed at lower COHb levels, but blood measurements were not accurate.	Schulte
High concentrations of CO were administered for 30 to 120 seconds, and then 10 minutes was allowed for washout of alveolar CO before blood COHb was measured.	Exposure sufficient to produce blood COHb levels above 5 percent has been shown to place a physiologic stress on patients with heart disease.	Data rely on COHb levels produced rapidly after short exposure to high levels of CO; this is not necessarily comparable to exposure over a longer time period or under equilibrium conditions.	Ayres et al.

APPENDIX

CONVERSION BETWEEN VOLUME AND MASS UNITS OF CONCENTRATION

The physical state of gaseous air pollutants at atmospheric concentrations may be described by the ideal gas law:

$$pv = nRT \qquad (1)$$

where:
p = Absolute pressure of gas
v = Volume of gas
n = Number of moles of gas
R = Universal gas constant
T = Absolute temperature

The number of moles (n) may be calculated from the weight of pollutant (w) and its molecular weight (m) by:

$$n = \frac{w}{m} \qquad (2)$$

Substituting equation 2 into equation 1 and rearranging yields:

$$v = \frac{wRT}{pm} \qquad (3)$$

Parts per million refers to the volume of pollutant (v) per million volumes of air (V).

$$\text{ppm} = \frac{v}{10^6 V} \qquad (4)$$

Substituting equation (3) into equation (4) yields:

$$\text{ppm} = \frac{w}{V}\,\frac{RT}{pm10^6} \qquad (5)$$

Using the appropriate values for variables in equation 5 a conversion from volume to mass units of concentration for CO may be derived as shown below.

T = 298°K (25°C)
p = 1 atm
m = 28 g/mole
R = 8.21×10^{-2} ℓ-atom/mole °K

$$\text{ppm} = \frac{w(\text{g}) \times 10^3\ (\text{mg/g})}{V(\ell) \times 10^{-3} (\text{m}^3/\ell)}\ \frac{8.21 \times 10^{-2}\ (\ell\text{-atm/mole°K}) \times 298(\text{°K})}{1(\text{atm}) \times 28\ (\text{g/mole}) \times 10^6}$$

$1\ \text{mg/m}^3 = 0.87\ \text{ppm}$
$1\ \text{ppm} = 1.15\ \text{mg/m}^3$

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